10/715,547

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1225	((514/267) or (544/251)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2007/04/10 17:43
L2	102	L1 and (tyrphostin or imidazo)	US-PGPUB; USPAT	OR	OFF	2007/04/10 17:44

10/ 715,547

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 4	DEC 18	CA/CAplus patent kind codes updated
NEWS 5	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 6	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 7	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 8	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 9	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 10	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 11	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 12	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 13	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 14	JAN 29	PHAR reloaded with new search and display fields
NEWS 15	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 17	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 18	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 19	FEB 26	MEDLINE reloaded with enhancements
NEWS 20	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 21	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 22	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 23	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 24	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 25	MAR 16	CASREACT coverage extended
NEWS 26	MAR 20	MARPAT now updated daily
NEWS 27	MAR 22	LWPI reloaded
NEWS 28	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 29	MAR 30	INPADOCDB will replace INPADOC on STN
NEWS 30	APR 02	JICST-EPLUS removed from database clusters and STN

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that

specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:21:04 ON 10 APR 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:21:11 ON 10 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 APR 2007 HIGHEST RN 929600-10-2
DICTIONARY FILE UPDATES: 9 APR 2007 HIGHEST RN 929600-10-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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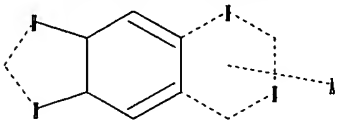
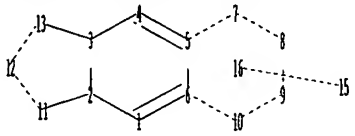
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10715547a.str



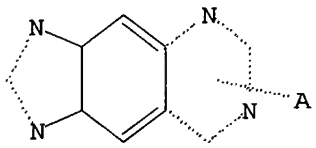


chain nodes :
15
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13
ring bonds :
1-2 1-6 2-3 2-11 3-4 3-13 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 12-13
exact/norm bonds :
1-2 1-6 2-3 2-11 3-4 3-13 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 12-13
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 15:CLASS 16:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful
FULL SEARCH INITIATED 17:21:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 10603 TO ITERATE

100.0% PROCESSED 10603 ITERATIONS 1146 ANSWERS
SEARCH TIME: 00.00.01

L2 1146 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	172.31

FILE 'HCAPLUS' ENTERED AT 17:21:46 ON 10 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 10 Apr 2007 VOL 146 ISS 16
FILE LAST UPDATED: 9 Apr 2007 (20070409/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

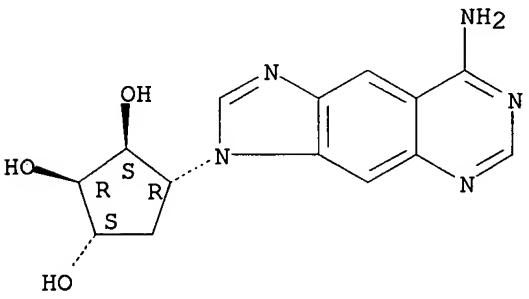
```
=> s l2
L3          137 L2

=> s l3 not py>2001
       6100666 PY>2001
L4           93 L3 NOT PY>2001

=> d l4 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 93 ANSWERS - CONTINUE? Y/(N):y

L4   ANSWER 1 OF 93  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2001:906602  HCAPLUS
DOCUMENT NUMBER:          136:177483
TITLE:                    Inhibition of measles virus replication by 5'-nor
                          carbocyclic adenosine analogues
AUTHOR(S):                Barnard, Dale L.; Stowell, Valerie D.; Seley,
                          Katherine L.; Hegde, Vishnumurthy R.; Das, Subha R.;
                          Rajappan, Vasanthakumar P.; Schneller, Stewart W.;
                          Smee, Donald F.; Sidwell, Robert W.
CORPORATE SOURCE:         Institute for Antiviral Research, Utah State
                          University, Logan, UT, USA
SOURCE:                   Antiviral Chemistry & Chemotherapy (2001), 12(4),
                          241-250
                          CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER:                International Medical Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Despite intense efforts to increase vaccine coverage, measles virus (MV)
     still causes significant morbidity and mortality in the world, sometimes
     as the result of severe, chronic, lethal disease.  In an effort to develop
     therapies to supplement immunization strategies, a number of 5'-nor
     carbocyclic adenosine analogs were evaluated for anti-MV activity in CV-1
     monkey kidney cells.  Of those compds. tested, those either unsubstituted
     at C4 or possessing a hydroxyl, azido or amino substituent at that
     position were the most active, with particularly significant inhibition of
     MV, strain Chicago-1.  The EC50 values against this strain ranged from
     <0.1 to 1 mg/mL, as determined by cytopathic effect reduction assay, and
confirmed
     by neutral red uptake.  By virus yield reduction assay (+)-(1S,2S,3R,4S)-4-(6'-
     amino-9'H-purin-9'-yl)cyclopentane-1,2,3-triol, (-)-(1R,2S,3R)-1-(6'-amino-
     9'H-purin-9'-yl)-2,3-dihydoxycyclopent-4-ene (I) (-)-(1R,2S,3R)-1-(6'-
     amino-9'H-purin-9'-yl)cyclopentane-2,3-dihydoxycyclopentane (II) and
     (-)-(1R,2R,3R,4S)-4-amino-1-(6'-amino-9'H-purin-9'-yl)cyclopentane-2,3-
     diol (III) were the most potent compds. tested, all with EC90 values of
     ≤0.4 mg/mL.  Compds. I and II were also tested against other MV
     strains, and similarly inhibited those strains except for four designated
     as Bil, Edmonston, SA and X-1108.  Compound III did not potently inhibit
     these other MV strains.  In addition, I, II and III demonstrated synergistic
     (additive) inhibition of MV replication in combination with ribavirin at
     several concns.  Compds. I, II and III were also potent MV inhibitors even
     when added to infected cells 24 h after virus exposure.  None of these
     three compds. was virucidal at concns. that inhibited viral replication as
     determined by virus yield reduction assay.  Most compds. tested were also not
toxic
     at concns. >100 mg/mL in actively growing and stationary-phase cells.
     Results suggest that these compds. may be clin. useful anti-MV virus
     agents.
IT   395066-40-7
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
```

(inhibition of measles virus replication by 5'-nor carbocyclic adenosine analogs)

RN 395066-40-7 HCAPLUS

CN 1,2,3-Cyclopentanetriol, 4-(8-amino-3H-imidazo[4,5-g]quinazolin-3-yl)-, (1S,2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:857046 HCAPLUS

DOCUMENT NUMBER: 136:194194

TITLE: KF31327, a new potent and selective inhibitor of cyclic nucleotide phosphodiesterase 5

AUTHOR(S): Hirose, Ryo; Okumura, Hiroshi; Yoshimatsu, Akiko; Irie, Junko; Onoda, Yasuo; Nomoto, Yuji; Takai, Haruki; Ohno, Tetsuji; Ichimura, Michio

CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co., Ltd., Nagaizumi-cho, Shizuoka, 411-8731, Japan

SOURCE: European Journal of Pharmacology (2001), 431(1), 17-24
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

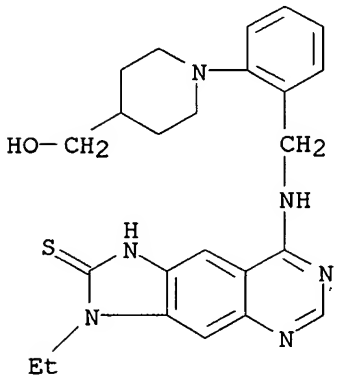
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of KF31327 (3-ethyl-8-[2-(4-hydroxymethylpiperidino)benzylamino]-2,3-dihydro-1H-imidazo[4,5-g]quinazoline-2-thione dihydrochloride) on phosphodiesterase 5 (cGMP-specific phosphodiesterase) activity and platelet aggregation were investigated and compared with those of sildenafil, a well-known phosphodiesterase 5 inhibitor. KF31327 inhibited phosphodiesterase 5 from canine trachea (Ki=0.16 nM) more potently than sildenafil (Ki=7.2 nM). The kinetic anal. revealed that KF31327 was a non-competitive inhibitor. In the presence of nitroglycerin (nitric oxide generator), both compds. inhibited the collagen-induced aggregation of rabbit platelets at less than 0.1 μM, augmenting intracellular cGMP level without affecting cAMP. In contrast, in the absence of nitroglycerin, a higher concentration (10 μM) of KF31327 was required to inhibit platelet aggregation and increased both cyclic nucleotide levels. However, 10 μM sildenafil did not affect aggregation despite elevation of cGMP comparable to that in the presence of nitroglycerin. These results indicate that in the presence of nitroglycerin, the inhibition of platelet aggregation by KF31327 is due to the elevation of cGMP, whereas the mechanism underlying the inhibition without nitroglycerin might be related to a rise in intracellular cAMP.

IT 204077-66-7, KF 31327
RL: PAC (Pharmacological activity); BIOL (Biological study)
(KF31327, a new potent and selective inhibitor of cyclic nucleotide phosphodiesterase 5)

RN 204077-66-7 HCAPLUS
CN 2H-Imidazo[4,5-g]quinazoline-2-thione, 3-ethyl-1,3-dihydro-8-[[[2-[4-(hydroxymethyl)-1-piperidinyl]phenyl]methyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

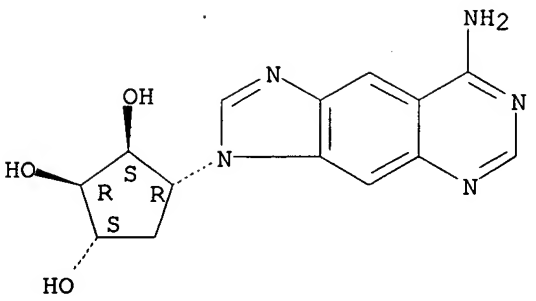


●2 HCl

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

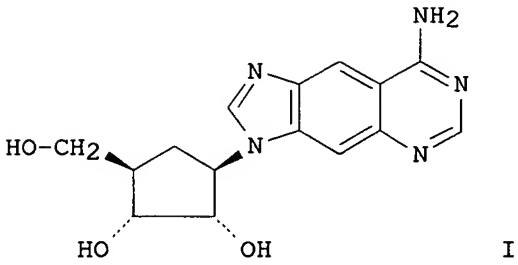
L4 ANSWER 3 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:780079 HCAPLUS
DOCUMENT NUMBER: 136:151379
TITLE: An 8-aminoimidazo[4,5-g]quinazoline carbocyclic nucleoside: a ring-extended analog of 5'-noraristeromycin
AUTHOR(S): Rajappan, Vasanthakumar P.; Schneller, Stewart W.
CORPORATE SOURCE: Department of Chemistry, Auburn University, Auburn, AL, 36849-5312, USA
SOURCE: Tetrahedron (2001), 57(44), 9049-9053
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antiviral properties of 5'-noraristeromycin (I) have been attributed to its inhibition of S-adenosylhomocysteine hydrolase. As part of an effort to establish the limiting structural parameters possible for the biol. properties of I, a ring-extended analog possessing 8-aminoimidazo[4,5-g]quinazoline as the base has been prepared and found to be less active than I.
IT 395066-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiviral activity of an aminoimidazoquinazoline carbocyclic nucleoside, a ring-extended analog of 5'-noraristeromycin)
RN 395066-40-7 HCAPLUS
CN 1,2,3-Cyclopentanetriol, 4-(8-amino-3H-imidazo[4,5-g]quinazolin-3-yl)-, (1S,2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

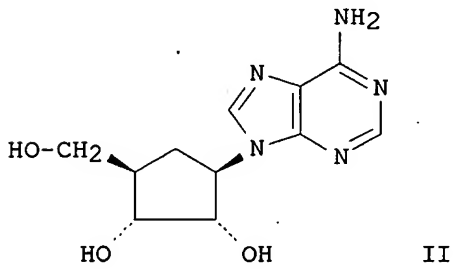


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:675149 HCAPLUS
DOCUMENT NUMBER: 136:20205
TITLE: Lin-benzoaristeromycin
AUTHOR(S): Rajappan, Vasanthakumar P.; Schneller, Stewart W.
CORPORATE SOURCE: Department of Chemistry, Auburn University, Auburn, AL, 36849, USA
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 1117-1121
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:20205
GI



I



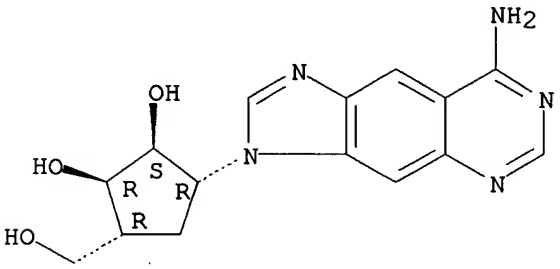
II

AB A synthesis and an antiviral anal. of the lin-benzoaristeromycin I linear extended derivative of aristeromycin II is described.

IT 379226-62-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiviral activity of lin-benzoaristeromycin)

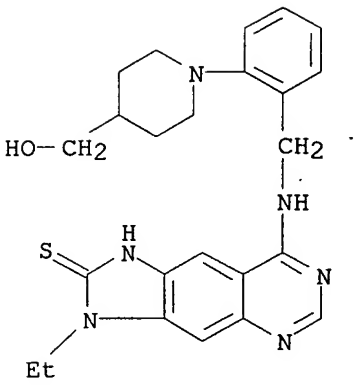
RN 379226-62-7 HCAPLUS
CN 1,2-Cyclopentanediol, 3-(8-amino-3H-imidazo[4,5-g]quinazolin-3-yl)-5-(hydroxymethyl)-, (1R,2S,3R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:555311 HCAPLUS
DOCUMENT NUMBER: 135:371655
TITLE: Research and development of synthetic processes for pharmaceuticals: Pursuit of rapid, inexpensive, and good processes
AUTHOR(S): Mohri, Shinichiro
CORPORATE SOURCE: Sakai Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Sakai, 590-8554, Japan
SOURCE: Yuki Gosei Kagaku Kyokaishi (2001), 59(5), 514-515
CODEN: YGKKAE; ISSN: 0037-9980
PUBLISHER: Yuki Gosei Kagaku Kyokai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 2 refs. on development of process for synthesis of KW-3433 as an angiotensin II receptor antagonist and KF31327 as a phosphodiesterase inhibitor.
IT 204077-66-7P, KF 31327
RL: SPN (Synthetic preparation); PREP (Preparation)
(research and development of synthetic processes for pharmaceuticals)
RN 204077-66-7 HCAPLUS
CN 2H-Imidazo[4,5-g]quinazoline-2-thione, 3-ethyl-1,3-dihydro-8-[[[2-[4-(hydroxymethyl)-1-piperidinyl]phenyl]methyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

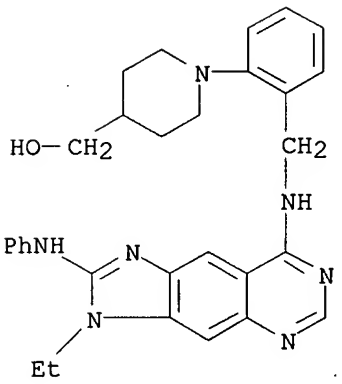


●2 HCl

L4 ANSWER 6 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:475249 HCAPLUS
DOCUMENT NUMBER: 135:212571
TITLE: Development of a Practical Synthetic Route of a PDE V Inhibitor KF31327
AUTHOR(S): Fujino, Kenji; Takami, Hitoshi; Atsumi, Toshiyuki; Ogasa, Takehiro; Mohri, Shin-ichiro; Kasai, Masaji
CORPORATE SOURCE: Sakai Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Sakai Osaka, 590-8554, Japan
SOURCE: Organic Process Research & Development (2001), 5(4), 426-433
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An efficient route suitable for a large-scale preparation of KF31327, a potent phosphodiesterase V inhibitor, has been developed. We selected 7-chloro-2,4(1H,3H)-quinazolinedione as a starting material, which gave the desired 6-nitro compound with good selectivity. In the chlorination of 7-ethylamino-6-nitro-2,4(1H,3H)-quinazolinedione, reaction conditions were optimized to minimize the amount of phosphorus oxychloride, and 2,4-dichloro-7-ethylamino-6-nitroquinazoline was obtained in excellent yield. After the selective substitution at C4 position, the chloro substituent at C2 position was successfully removed by hydrogenation concomitant with the reduction of nitro group. The construction of the imidazothione ring was achieved by using Ph isothiocyanate as a thiocarbonyl donor instead of extremely flammable carbon disulfide. Multikilograms of drug substance have been successfully prepared by these procedures.

IT 357670-23-6P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct; in preparation of KF31327)
RN 357670-23-6 HCAPLUS
CN 4-Piperidinemethanol, 1-[2-[[[3-ethyl-2-(phenylamino)-3H-imidazo[4,5-g]quinazolin-8-yl]amino]methyl]phenyl]- (9CI) (CA INDEX NAME)



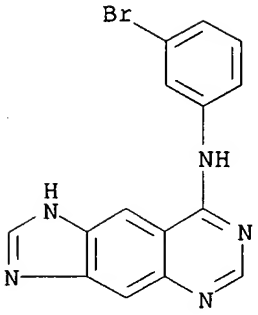
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:872652 HCAPLUS
DOCUMENT NUMBER: 134:202418
TITLE: Allosteric inhibition of fructose-1,6-bisphosphatase by anilinoquinazolines
AUTHOR(S): Wright, S. W.; Hageman, D. L.; McClure, L. D.; Carlo, A. A.; Treadway, J. L.; Mathiowetz, A. M.; Withka, J. M.; Bauer, P. H.
CORPORATE SOURCE: Pfizer Central Research, Groton, CT, 06340, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), Volume Date 2001, 11(1), 17-21
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Anilinoquinazolines currently of interest as inhibitors of tyrosine kinases have been found to be allosteric inhibitors of the enzyme fructose 1,6-bisphosphatase. These represent a new approach to inhibition of F16BPase and serve as leads for further drug design. Enzyme inhibition is achieved by binding at an unidentified allosteric site.

IT 171179-32-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(allosteric inhibition of fructose bisphosphatase by anilinoquinazolines)

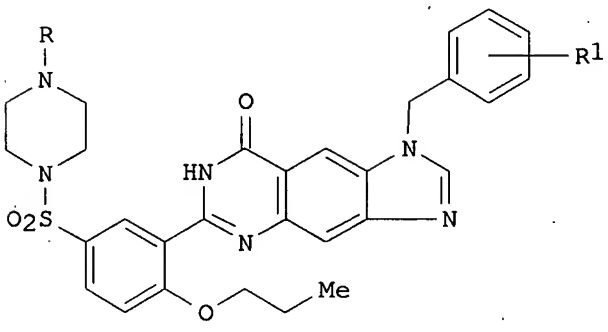
RN 171179-32-1 HCAPLUS
CN 1H-Imidazo[4,5-g]quinazolin-8-amine, N-(3-bromophenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:818584 HCAPLUS
DOCUMENT NUMBER: 134:115917
TITLE: Optimization of Substituted N-3-Benzylimidazoquinazolinone Sulfonamides as Potent and Selective PDE5 Inhibitors
AUTHOR(S): Rotella, David P.; Sun, Zhong; Zhu, Yeheng; Krupinski, John; Pongrac, Ronald; Seliger, Laurie; Normandin, Diane; Macor, John E.
CORPORATE SOURCE: Departments of Discovery Chemistry and Metabolic and Cardiovascular Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-5400, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(26), 5037-5043
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:115917
GI



I

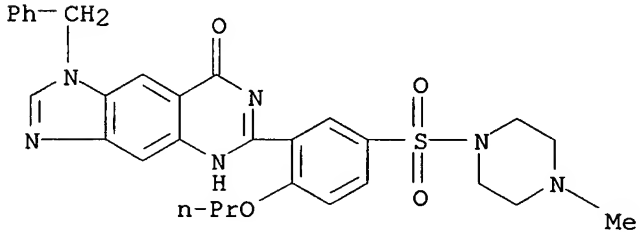
AB A previous report identified the N-3-benzylimidazoquinazolinone nucleus as a more selective PDE5 inhibitor template compared to the pyrazolopyrimidine of sildenafil. This paper describes in detail the structure-activity relationships of a set of sulfonamide analogs, such as I (R = Me, R1 = 4-F; R = Et, R1 = H, 2-Cl, 2-MeO, 3-F, 3-MeO, 4-F), several of which are both more potent and more selective PDE5 inhibitors in vitro than sildenafil. The synthesis, in vitro enzyme activity and

selectivity, and in vitro functional and preclin. pharmacokinetic assessment of mols. in this series are described.

IT 252231-99-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of substituted N-3-benzylimidazoquinazolinone sulfonamides as potent and selective PDE5 inhibitors)

RN 252231-99-5 HCAPLUS

CN Piperazine, 1-[[3-[5,8-dihydro-8-oxo-1-(phenylmethyl)-1H-imidazo[4,5-g]quinazolin-6-yl]-4-propoxyphenyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)



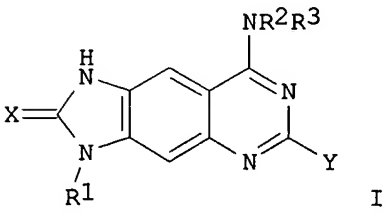
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:612064 HCAPLUS
DOCUMENT NUMBER: 133:193165
TITLE: Preparation of imidazoquinazolines and cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase inhibitors
INVENTOR(S): Onoda, Yasuo; Machii, Daisuke; Nomoto, Yuji; Takai, Haruki; Ono, Satoshi; Ichimura, Michiaki
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000239277	A	20000905	JP 1999-41567	19990219

PRIORITY APPLN. INFO.: JP 1999-41567 19990219
OTHER SOURCE(S): MARPAT 133:193165
GI



I

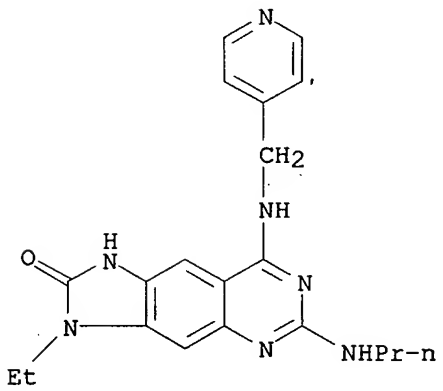
AB Title compds. I [R1 = lower alkyl cycloalkyl, lower alkenyl, aralkyl,

aryl, etc.; R2, R3 = H, alkyl, cycloalkyl, lower alkenyl, aralkyl, aryl, etc.; X = O, S; Y = OR4, SR5, NR6R7; R4, R5 = lower alkyl, cycloalkyl, lower alkenyl, aralkyl, etc.; R6, R7 = H, lower alkyl, cycloalkyl, alkenyl, aralkyl, aryl, etc.; R6R7 = N-containing heterocyclic ring]. 7-Ethylamino-6-nitro-2-propylamino-4-(4-pyridylmethylamino)quinazoline was hydrogenated with Pd/C in EtOH-THF mixture for 8 h and reacted with CS2 in the presence of Et3N in EtOH at room temperature overnight to give 65% 3-ethyl-6-propylamino-8-(4-pyridylmethylamino)-2,3-dihydro-1H-imidazo[4,5-g]quinazoline-2-thione, which was treated with HCl in AcOEt to give their HCl salt showing good antihypertensive activity.

IT 289660-45-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of imidazoquinazolines and cyclic guanosine monophosphate-specific phosphodiesterase inhibitors)

RN 289660-45-3 HCAPLUS

CN 2H-Imidazo[4,5-g]quinazolin-2-one, 3-ethyl-1,3-dihydro-6-(propylamino)-8-[(4-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)



L4 ANSWER 10 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:176119 HCAPLUS

DOCUMENT NUMBER: 132:342802

TITLE: N-3-Substituted Imidazoquinazolinones: Potent and Selective PDE5 Inhibitors as Potential Agents for Treatment of Erectile Dysfunction

AUTHOR(S): Rotella, David P.; Sun, Zhong; Zhu, Yeheng; Krupinski, John; Pongrac, Ronald; Seliger, Laurie; Normandin, Diane; Macor, John E.

CORPORATE SOURCE: Discovery Chemistry and Cardiovascular Drug Discovery, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-5400, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(7), 1257-1263
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

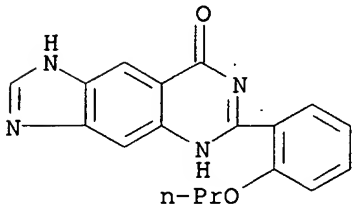
AB Phosphodiesterase type 5 (PDE5) inhibitors with improved PDE isoenzyme selectivity relative to sildenafil (Viagra) may result in agents for the treatment of male erectile dysfunction (MED) with a lower incidence of PDE-associated adverse effects. This paper describes the discovery of a PDE5

inhibitor with improved potency and selectivity in vitro compared to sildenafil.

IT 252231-68-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of imidazoquinazolinones as potent and selective PDE5 inhibitors and potential agents for treatment of erectile dysfunction)

RN 252231-68-8 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro-6-(2-propoxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:782032 HCAPLUS
Correction of: 1996:73866

DOCUMENT NUMBER: 131:351298
Correction of: 124:232395

TITLE: Tyrosine kinase inhibitors. 9. Synthesis and evaluation of fused tricyclic quinazoline analogs as ATP site inhibitors of the tyrosine kinase activity of the epidermal growth factor receptor

AUTHOR(S): Rewcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.

CORPORATE SOURCE: School of Medicine, University of Auckland, Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 918-928
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results

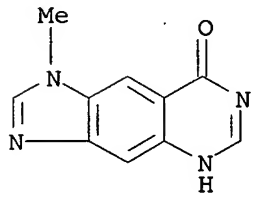
are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared And evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear

imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

IT 171179-64-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate in preparation of imidazoquinazolines as tyrosine kinase inhibitors)

RN 171179-64-9 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro-1-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:777760 HCAPLUS

DOCUMENT NUMBER: 132:87758

TITLE: Tyrosine Kinase Inhibitors. 16. 6,5,6-Tricyclic Benzothieno[3,2-d]pyrimidines and Pyrimido[5,4-b]- and -[4,5-b]indoles as Potent Inhibitors of the Epidermal Growth Factor Receptor Tyrosine Kinase

AUTHOR(S): Showalter, H. D. Hollis; Bridges, Alexander J.; Zhou, Hairong; Sercel, Anthony D.; McMichael, Amy; Fry, David W.

CORPORATE SOURCE: Departments of Chemistry and Cancer Research, Parke-Davis Pharmaceutical Research Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(26), 5464-5474
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

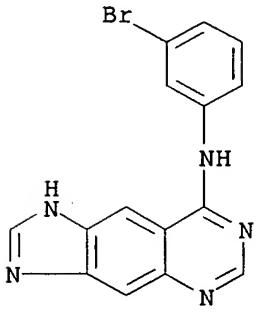
AB Several elaborations of the fundamental anilinopyrimidine pharmacophore have been reported as potent and selective inhibitors of the epidermal growth factor receptor (EGFr) tyrosine kinase. This paper reports on a

series of inhibitors whereby some 6,5-bicyclic heteroarom. systems were fused through their C-2 and C-3 positions to this anilinopyrimidine pharmacophore. Although the resulting tricycles did not produce the enormous potency of some of the (5/6),6,6-bicyclic systems, the best of them had IC50s for the EGFr TK around 1 nM. Investigation of 4-position side chains in the indolopyrimidines confirmed that m-bromoaniline was an optimal substituent for potency. Investigation of substitution within the C-(benzo)ring of benzothienopyrimidines confirmed that introduction of an extra ring can change sharply the effects of substituents when compared to similar bicyclic nuclei, and only two substituents were found which even moderately enhanced inhibitory activity over the parent compound for this series.

IT 171179-32-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of benzothieno-, pyrimido- and indolo-pyrimidines as inhibitors of epidermal growth factor receptor tyrosine kinase)

RN 171179-32-1 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazolin-8-amine, N-(3-bromophenyl)- (9CI) (CA INDEX NAME)



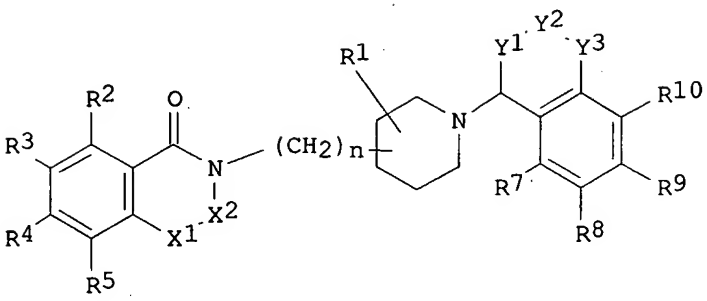
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:690958 HCAPLUS
DOCUMENT NUMBER: 131:299459
TITLE: Preparation of quinazoline derivatives and other heterocyclic compounds as analgesics
INVENTOR(S): Shimada, Junichi; Shirai, Tomomi; Okamura, Yuko; Kosaka, Nobuo
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

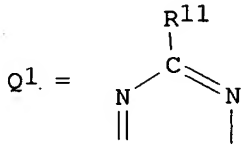
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953924	A1	19991028	WO 1999-JP1982	19990414

W: AU, BG, BR, CA, CN, CZ, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: JP 1998-107681 A 19980417
OTHER SOURCE(S): MARPAT 131:299459
GI



I

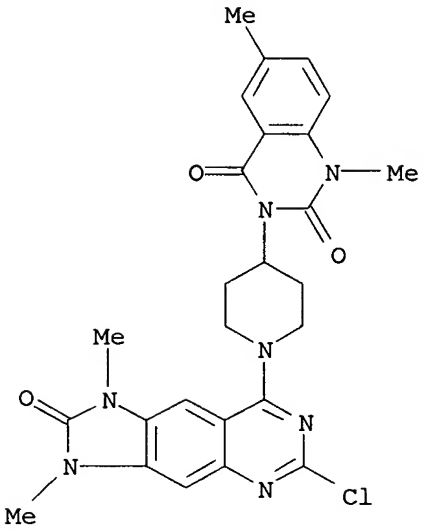


AB The title compds. I [R1 represents hydrogen, lower alkyl, etc.; R2 to R5 each represents hydrogen, lower alkyl, halogeno, etc.; n is 0 to 2; X1-X2 represents a group represented by formula NR6CO or N:X3 ; R6 represents hydrogen, lower alkyl, etc. and X3 represents N or CR15; R15 represents hydrogen, lower alkyl, etc.; Y1-Y2-Y3 represents a group represented by formula Q1 (wherein R11 represents hydrogen, lower alkyl, hydroxyl, etc.), etc.; and R7 to R10 each represents hydrogen, lower alkoxy, etc.] are prepared Formulations containing I are given. 3-[1-(6,7-Dimethoxy-4-quinazolinyl)-4-piperidyl]-3,4-dihydro-6-methyl-4-oxoquinazoline at 10 μg/rat showed analgesic effect in rats.

IT 222423-42-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. and other heterocyclic compds. as analgesics)

RN 222423-42-9 HCAPLUS

CN 2,4(1H,3H)-Quinazolinedione, 3-[1-(6-chloro-2,3-dihydro-1,3-dimethyl-2-oxo-1H-imidazo[4,5-g]quinazolin-8-yl)-4-piperidinyl]-1,6-dimethyl- (9CI) (CA INDEX NAME)

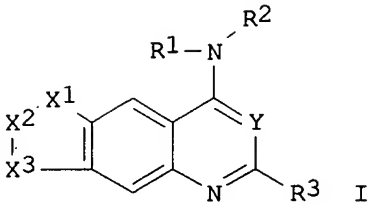


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:566045 HCAPLUS
DOCUMENT NUMBER: 131:199702
TITLE: Preparation of imidazoquinazoline derivatives or analogs thereof for treatment of erectile dysfunction
INVENTOR(S): Onoda, Yasuo; Takami, Hitoshi; Seishi, Takashi; Machii, Daisuke; Nomoto, Yuji; Takai, Haruki; Okumura, Hiroshi; Ohno, Tetsuji; Yamada, Koji; Ichimura, Michio
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943674	A1	19990902	WO 1999-JP920	19990226
W: AU, BG, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9926411	A	19990915	AU 1999-26411	19990226
PRIORITY APPLN. INFO.:			JP 1998-48329 A	19980227
			WO 1999-JP920 W	19990226

OTHER SOURCE(S): MARPAT 131:199702
GI



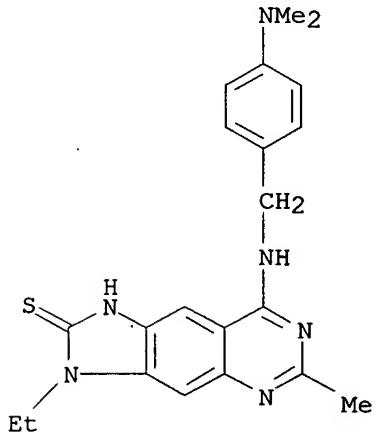
I

AB The title compds. I [R1, R2 = H, (un)substituted alkyl, etc.; R3 = H, (un)substituted alkyl, etc.; Y represents N or CH; X1X2X3 represents N:NNR7, NHC(:NCN)NR7, etc.; R7 = H, (un)substituted alkyl, etc.] are prepared Formulations containing a compound of this invention are given. I have a potent and selective cGMP-specific phosphodiesterase (PDE) inhibitory effect and are useful in treating or relieving sexual impotence, etc. The title compound I.2HCl [X1X2X3 = NHC(:S)N(Et); Y = N; R1 = 4-dimethylaminobenzyl; R2 = H; R3 = methyl] in vitro at 1 nM gave 86% inhibition of PDE V.

IT 241815-12-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazoquinazoline derivs. or analogs thereof for treatment of erectile dysfunction)

RN 241815-12-3 HCAPLUS

CN 2H-Imidazo[4,5-g]quinazoline-2-thione, 8-[[[4-(dimethylamino)phenyl]methyl]amino]-3-ethyl-1,3-dihydro-6-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:409238 HCAPLUS

DOCUMENT NUMBER: 131:97601

TITLE: Piperidine derivatives for increasing erythropoiesis.

INVENTOR(S): Shimada, Junichi; Sugimoto, Seiji; Okamura, Yuko; Yamashita, Koji; Tamaoki, Tatsuya

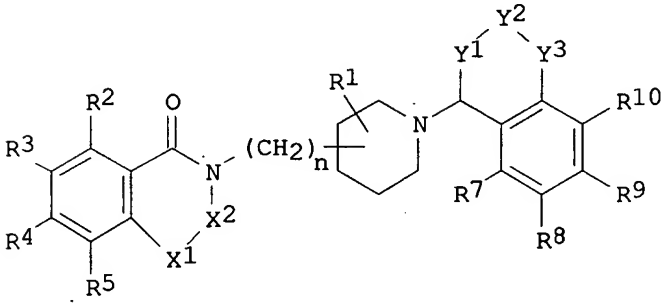
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 65 pp.

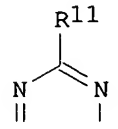
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11171774	A	19990629	JP 1997-335723	19971205

PRIORITY APPLN. INFO.: JP 1997-335723 19971205
OTHER SOURCE(S): MARPAT 131:97601
GI



I



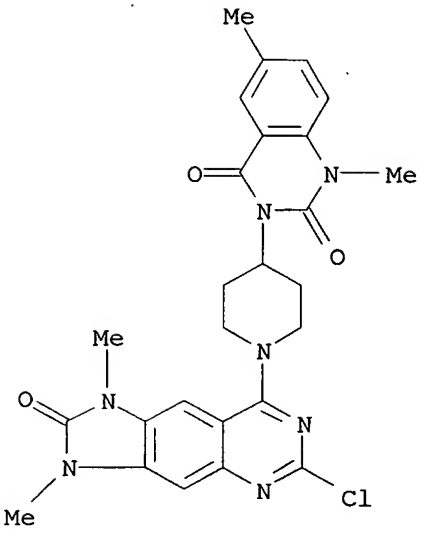
II

AB Piperidine derivs. (I; R1 = H, low alkyl, halogen; R2, R3, R4, R5 = H, halogen, amino; n = 0-2; X1-X2 = R6-N-CO-, -N=X3, X3 = N, C-R15, with R6 and R15 = H, low alkyl, low alkenyl; Y1-Y3 = II, with R11 = H, low alkyl, OH; R7, R8, R9, R10 = H, low alkyl, OH) and their pharmacol. acceptable salts are claimed for increasing erythropoiesis especially in hemodialysis to prevent anemia. Formulation examples of I tablets, capsules, injections, and rectum suppositories were given.

IT 222423-42-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(piperidine derivs. for increasing erythropoiesis)

RN 222423-42-9 HCAPLUS

CN 2,4(1H,3H)-Quinazolinedione, 3-[1-(6-chloro-2,3-dihydro-1,3-dimethyl-2-oxo-1H-imidazo[4,5-g]quinazolin-8-yl)-4-piperidinyl]-1,6-dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:271355 HCAPLUS
DOCUMENT NUMBER: 130:281996
TITLE: Preparation of piperidine derivatives as adenosine uptake inhibitors
INVENTOR(S): Okamura, Yuko; Fujiwara, Shigeki; Sasaki, Shin-ichi; Yao, Kozo; Nonaka, Hiromi; Karasawa, Akira; Suzuki, Koji
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9919326	A1	19990422	WO 1998-JP4664		19981015
W: AU, BG, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9894620	A	19990503	AU 1998-94620		19981015
PRIORITY APPLN. INFO.:			JP 1997-281769	A	19971015
			WO 1998-JP4664	W	19981015

OTHER SOURCE(S): MARPAT 130:281996
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

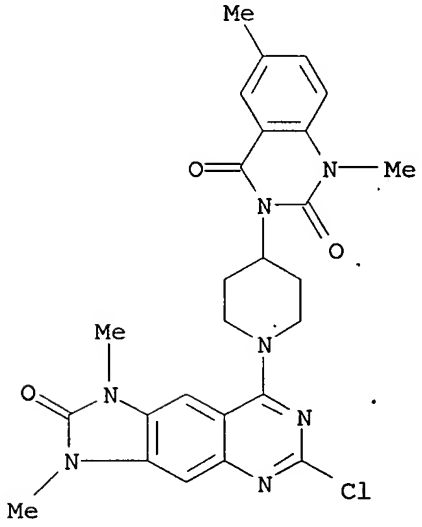
AB Piperidine derivs. I (R1 = H, alkyl, halo; R2, R3, R4, R5 = H, halo, amino, alkylamino, alkanoylamino, NO2, cyano, alkyl, OH, alkoxy, alkylthio, carboxy, alkoxycarbonyl, alkanoyl, aralkyloxy, alkanoyloxy; n = 0, 1, 2; X-Y = R6NCOMe, N:CMeR7; R6 = H, alkyl, alkenyl, aryl, aralkyl; R7 = H, OH, alkyl, alkenyl, aryl, aralkyl, alkylthio; Q = Q1, Q2, Q3, Q4, Q5;

R8, R9 = H, alkyl, alkenyl, aryl, aralkyl; R10 = H, alkyl, OH, alkoxy, aryl, halo, amino; R11 = H, alkyl, cyano, carboxy, alkoxycarbonyl; Z = O, S) and their pharmacol. acceptable salts were prepared In an in vitro test for inhibition of incorporation of [3H]-adenosine into erythrocytes, 2,3-dihydro-5-[4-(1,2,3,4-tetrahydro-1,6-dimethyl-2,4-dioxoquinazolin-3-yl)-1-piperidinyl]-1,3-dimethyl-8-morpholino-1H-imidazo[4,5-g]phthalazine-2-one showed IC50 of 15 nM.

IT 222423-42-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine derivs. as adenosine uptake inhibitors)

RN 222423-42-9 HCAPLUS

CN 2,4(1H,3H)-Quinazolinedione, 3-[1-(6-chloro-2,3-dihydro-1,3-dimethyl-2-oxo-1H-imidazo[4,5-g]quinazolin-8-yl)-4-piperidinyl]-1,6-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

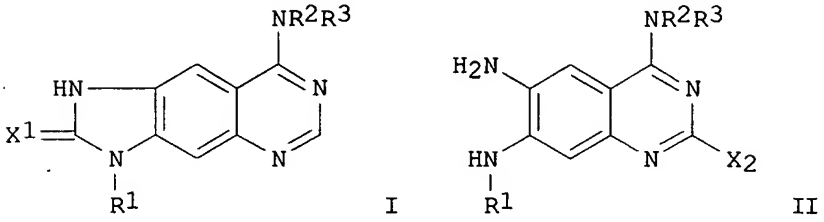
L4 ANSWER 17 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1999:39911 HCAPLUS
DOCUMENT NUMBER:	130:139355
TITLE:	Method of manufacturing imidazoquinazolines by cyclocondensation of 6,7-diaminoquinazolines with isothiocyanate
INVENTOR(S):	Fujino, Kenji; Takami, Hitoshi; Makai, Ayako; Mouri, Shinichiro; Ogasa, Takehiro; Ichimura, Michiaki; Kasai, Seiji
PATENT ASSIGNEE(S):	Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 13 pp. CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 11005794 A 19990112 JP 1998-105945 19980416
PRIORITY APPLN. INFO.: JP 1997-106028 A 19970423
OTHER SOURCE(S): CASREACT 130:139355; MARPAT 130:139355
GI



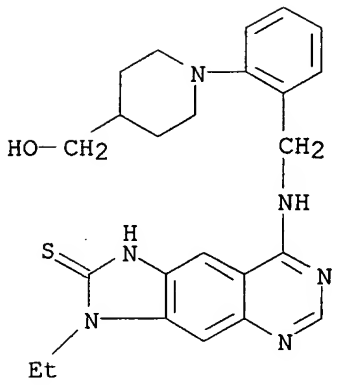
I II

AB Imidazoquinazolines [I; R1 = H, (un)substituted lower alkyl, bicycloalkyl, lower alkenyl, alkanoyl, aryl, heteroaryl, aralkyl, or heteroarylalkyl; R2, R3 = H, (un)substituted lower alkyl, bicycloalkyl, benzocycloalkenyl, lower alkenyl, aryl, heteroaryl, aralkyl, or heteroarylalkyl; or NR2R3 = (un)substituted heterocyclyl; X1 = S, O; X2 = alkylsulfonyloxy, (un)substituted arylsulfonyloxy, halo] or salts thereof are prepared by reaction of 6,7-diaminoquinazolines (II; R1, R2, R3 = same as above) or salts thereof with isothiocyanic acid derivs. These compds. I possess cyclic guanosine 3',5'-monophosphate (cGMP)-specific phosphodiesterase V (PDE V) inhibiting activity and are useful for treating or alleviating cardiovascular diseases such as hypertension (no data). Thus, 4.7 mL Ph isothiocyanate was added dropwise over 5 h to a suspension of 7.5 g 6-amino-7-(ethylamino)-4-[2-[4-(hydroxymethyl)piperidino]benzylamino]quinazoline (preparation given) in 155 mL 1-propanol with stirring under reflux and after the reaction, the stirring was continued for 2 h at 20° to give the title 1H-imidazo[4,5-g]quinazoline-2-thione, I [X1 = S, X2 = H, R1 = Et, R2 = 2-[4-(hydroxymethyl)piperidino]benzyl, R3 = H]. I [X1 = O, X2 = Cl, R1 = Et, R2 = 4-(dimethylamino)benzyl, R3 = H] in vitro inhibited 69% PDE V at 1 nM.

IT 204077-66-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazoquinazolines as cardiovascular agents by cyclocondensation of diaminoquinazolines with isothiocyanate)

RN 204077-66-7 HCAPLUS

CN 2H-Imidazo[4,5-g]quinazoline-2-thione, 3-ethyl-1,3-dihydro-8-[[[2-[4-(hydroxymethyl)-1-piperidinyl]phenyl]methyl]amino]-, hydrochloride (1:2) (CA INDEX NAME)

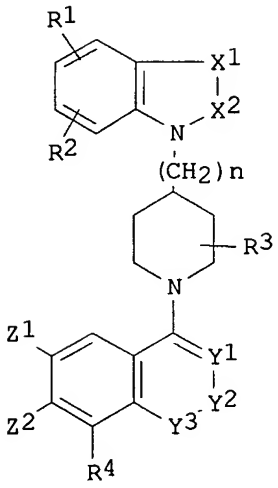


●2 HCl

L4 ANSWER 18 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:795478 HCAPLUS
DOCUMENT NUMBER: 130:95479
TITLE: Preparation of piperidine derivatives as cell adhesion inhibitors for inflammation inhibitors, metastasis inhibitors, etc.
INVENTOR(S): Sasaki, Shinichi; Fujiwara, Shigeki; Hagiwara, Koji; Takai, Haruki; Suzuki, Koji; Miki, Ichiro; Hisano, Yukako; Kase, Hiroshi
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 37 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10330377	A	19981215	JP 1997-144105	19970602
PRIORITY APPLN. INFO.:			JP 1997-144105	19970602

OTHER SOURCE(S): MARPAT 130:95479
GI



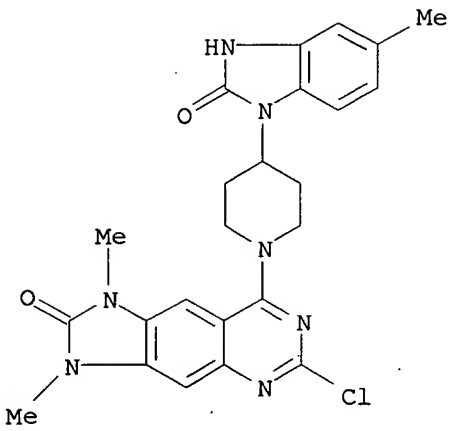
I

AB The derivs. I [R1 = (un)substituted lower alkyl, OH, lower alkoxy, carboxy, lower alkoxycarbonyl, lower alkylcarbonyl, lower alkoxycarbonyl, (un)substituted aryl, (un)substituted aryloxy, (un)substituted aryloxycarbonyl, (un)substituted arylcarbonyl, carbamoyl, mono- or di-lower alkylcarbamoyl, mono- or di-arylcarbamoylNO2, halo; R2 = H, any group given for R1; R3 = H, lower alkyl; R4 = H, lower alkyl, lower alkoxy; X1X2 = N:N, NCR5 (R5 = H, lower alkyl, lower alkoxy), NR6W [R6 = H, (un)substituted lower alkyl, (un)substituted aryl; W = CO, CS, SO2], OCR7 (R7 = O, S); Y1Y2Y3 = :NCR8:N [R8 = H, lower alkoxy, halo, amino, mono- or di-(un)substituted lower alkyl-amino, (un)substituted aliphatic heterocyclyl], :NN:CR8A (R8A = any group given for R8), :NCR8B:CH (R8B = any group given for R8), :C(COR9)CH:N [R9 = H, OH, lower alkyl, lower alkoxy, (un)substituted aryl, (un)substituted aryloxy, amino, mono- or di-lower alkyl-amino, mono- or di-(un)substituted aryl-amino, (un)substituted aliphatic heterocyclyl]; Z1, Z2 = H, (un)substituted lower alkyl, OH, lower alkoxy, carboxy, lower alkoxycarbonyl, lower alkylcarbonyl, carbamoyl, mono- or di-lower alkyl-carbamoyl, halo, NO2; Z1 and Z2 may be bonded to each other to form NR10CXN R11 (R10, R11 = H, lower alkyl; X = O, S); n = 0, 1, 2] or their pharmacol. acceptable salts are prepared I inhibit cell adhesion, especially between HUVEC and HL60 leukemia cell, thus being useful as inflammation inhibitors, antiallergic drugs, metastasis inhibitors, immunosuppressants, etc. 2,3-Dihydro-5-methyl-1-(4-piperidinyl)-1H-benzimidazol-2-one was treated with Et 4-chloro-6-methoxyquinoline-3-carboxylate to give Et 4-[4-(2,3-dihydro-5-methyl-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]-6-methoxyquinoline-3-carboxylate. This inhibited TNFα-stimulated adhesion of HL60 cells to HUVEC with inhibition rates 108 and 51% at 10-5 and 10-6M, resp.

IT 219324-42-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine derivs. as cell adhesion inhibitors for inflammation inhibitors and metastasis inhibitors)

RN 219324-42-2 HCAPLUS

CN 2H-Imidazo[4,5-g]quinazolin-2-one, 6-chloro-8-[4-(2,3-dihydro-5-methyl-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]-1,3-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

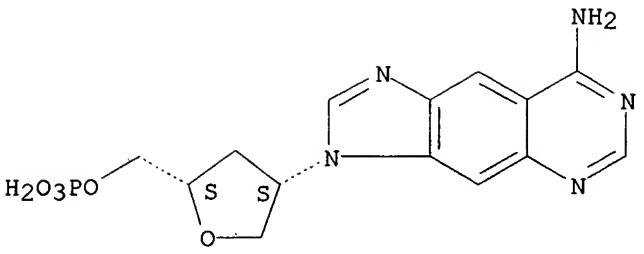


L4 ANSWER 19 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:515947 HCAPLUS
DOCUMENT NUMBER: 129:290347
TITLE: Inhibition of HIV integrase by novel nucleotides bearing tricyclic bases
AUTHOR(S): Zhang, Jianzhong; Neamati, Nouri; Pommier, Yves; Nair, Vasu
CORPORATE SOURCE: Department of Chemistry, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(14), 1887-1890
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 5'-Monophosphates of several novel dideoxynucleosides bearing tricyclic nucleobases were synthesized. Both linear and angular ring-extended analogs of isomeric dideoxyadenosine 5'-monophosphate were discovered to have moderate to good inhibition of the viral-encoded enzyme, HIV integrase. The results suggest that the nucleotide binding site of HIV integrase can accommodate major modifications in the nucleobase, which is in stark contrast to the nucleotide binding site on HIV reverse transcriptase.

IT 214121-26-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of tricyclic base nucleotides as inhibitor of HIV integrase)
RN 214121-26-3 HCAPLUS
CN D-threo-Pentitol, 2-(8-amino-3H-imidazo[4,5-g]quinazolin-3-yl)-1,4-anhydro-2,3-dideoxy-, 5-(dihydrogen phosphate), disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 Na

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:505889 HCAPLUS
Correction of: 1996:73866
DOCUMENT NUMBER: 129:109067
Correction of: 124:232395
TITLE: Tyrosine kinase inhibitors. 9. Synthesis and evaluation of fused tricyclic quinazoline analogs as ATP site inhibitors of the tyrosine kinase activity of the epidermal growth factor receptor
AUTHOR(S): Rewcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.
CORPORATE SOURCE: School of Medicine, University of Auckland, Auckland, 92019, N. Z.
SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 918-928
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

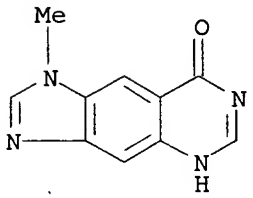
AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazó[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-

g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR. Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

IT 171179-64-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate in preparation of imidazoquinazolines as tyrosine kinase inhibitors)

RN 171179-64-9 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro-1-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:163595 HCAPLUS

DOCUMENT NUMBER: 128:217377

TITLE: Preparation and formulation of imidazoquinazoline derivatives as cGMP-phosphodiesterase inhibitors

INVENTOR(S): Onoda, Yasuo; Nomoto, Yuji; Ohno, Tetsuji; Yamada, Koji; Ichimura, Michio

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2

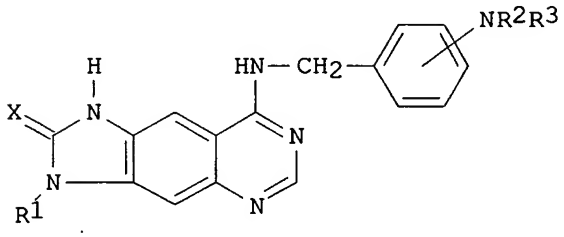
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

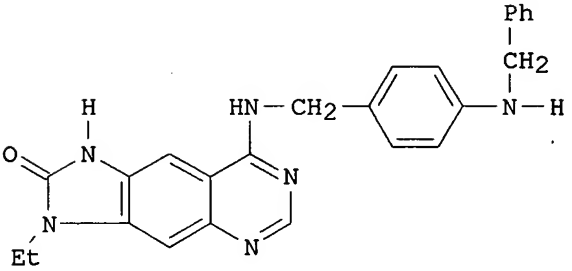
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808848	A1	19980305	WO 1997-JP3023	19970829
W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2236012	A1	19980305	CA 1997-2236012	19970829
AU 9740323	A	19980319	AU 1997-40323	19970829
AU 724809	B2	20000928		
EP 863144	A1	19980909	EP 1997-937841	19970829
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1205008	A	19990113	CN 1997-191339	19970829
HU 9900790	A2	19990628	HU 1999-790	19970829
NZ 330292	A	20000128	NZ 1997-330292	19970829
US 6127541	A	20001003	US 1998-65061	19980427
MX 9803347	A	20000831	MX 1998-3347	19980428
NO 9801946	A	19980629	NO 1998-1946	19980429
PRIORITY APPLN. INFO.:			JP 1996-230807 A	19960830
			WO 1997-JP3023 W	19970829

OTHER SOURCE(S): MARPAT 128:217377
GI



I



II

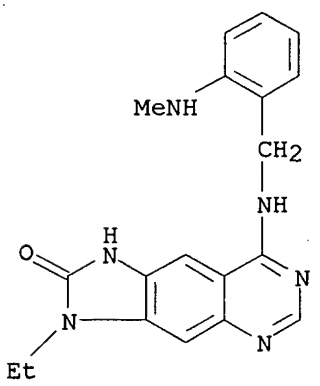
AB The title compds. I [R1 represents hydrogen, optionally substituted lower alkyl, optionally substituted cycloalkyl, optionally substituted bicycloalkyl, optionally substituted tricycloalkyl, etc.; R2 represents hydrogen, optionally substituted lower alkyl, optionally substituted cycloalkyl, optionally substituted bicyclaolkyl, optionally substituted tricycloalkyl, optionally substituted lower alkenyl, optionally substituted aralkyl, etc.; R3 represents hydrogen, optionally substituted lower alkyl, optionally substituted cycloalkyl, optionally substituted

bicycloalkyl, optionally substituted tricycloalkyl, optionally substituted lower alkenyl, optionally substituted aralkyl, etc., or R2 and R3 may form together with N an optionally substituted heterocyclic group; and X represents O or S] are prepared I have selective inhibitory effects on cGMP-specific phosphodiesterase and are useful in, for example, treating or relieving cardiovascular diseases such as thrombosis, angina pectoris, hypertension, cardiac insufficiency and arteriosclerosis, asthma, etc. and treating sexual impotence. In an in vitro test, the title compound II at 1 nM gave 62% inhibition of cGMP-phosphodiesterase.

IT 204077-32-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazoquinazoline derivs. as cGMP-phosphodiesterase inhibitors)

RN 204077-32-7 HCAPLUS

CN 2H-Imidazo[4,5-g]quinazolin-2-one, 3-ethyl-1,3-dihydro-8-[[[2-(methylamino)phenyl]methyl]amino]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:757851 HCAPLUS
DOCUMENT NUMBER: 128:13390
TITLE: Synthesis of new dideoxynucleosides bearing ring-extended nucleobases
AUTHOR(S): Zhang, Jianzhong; Nair, Vasu
CORPORATE SOURCE: Department of Chemistry, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Nucleosides & Nucleotides (1997), 16(7-9), 1091-1094
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New dideoxynucleosides where the nucleobase is lin-benzoadenine is reported. The key target compound, (S,S)-isodideoxybenzoadenosine, is stable with respect to hydrolytic cleavage of the glycosyl bond and it is a poor substrate for adenosine deaminase. Its monophosphate is not a substrate for AMP deaminase.

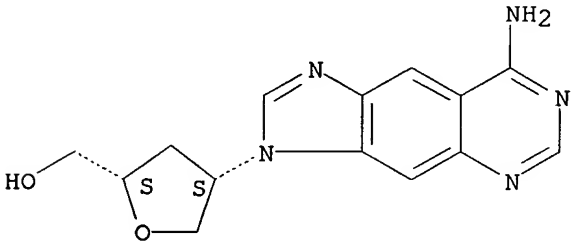
IT 199009-38-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of new dideoxynucleosides bearing ring-extended nucleobases)

RN 199009-38-6 HCAPLUS

CN D-threo-Pentitol, 2-(8-amino-3H-imidazo[4,5-g]quinazolin-3-yl)-1,4-anhydro-2,3-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:210842 HCAPLUS

DOCUMENT NUMBER: 126:182991

TITLE: A Model of the Interaction of Substrates and Inhibitors with Xanthine Oxidase

AUTHOR(S): Rastelli, Giulio; Costantino, Luca; Albasini, Albano

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Modena, Modena, 41100, Italy

SOURCE: Journal of the American Chemical Society (1997), 119(13), 3007-3016
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

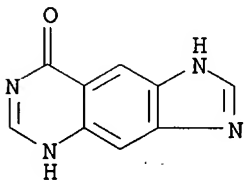
AB A model of the interaction of substrates and inhibitors with xanthine oxidase (XO) based on similarity concepts and mol. modeling is introduced and discussed, and previous literature is reexamd. in the light of recent insights into the mechanism and structure of XO. Use is made of quantum-chemical calcns. with the inclusion of solvent effects, mol. superimposition with least-squares fitting algorithms, and mol. electrostatic potentials. First, the relative stabilities of the tautomeric forms of the physiol. substrates, xanthine and hypoxanthine, are calculated both in vacuo and in water to select the most abundant form(s) at physiol. pH: the two substrates prove to be stable in their lactam forms, with a dominance of the N7-H tautomer for xanthine and of N9-H for hypoxanthine. The structures of xanthine and hypoxanthine are then superimposed, and their relative orientation with respect to the molybdenum center of XO is suggested. The criteria used for superimposition reflect the importance of functional groups of xanthine and hypoxanthine, as inferred from exptl. work. In particular, the carbonyl oxygen common to the two substrates is given special consideration on account of its determinant role. The results show that the most important functional groups of the two substrates can be successfully superimposed by means of a rotation that exchanges the five-membered with the six-membered rings of xanthine and hypoxanthine with respect to molybdenum. The close similarity of the electrostatic potentials of the two superimposed mols. adds weight to the proposed

orientation of the substrates in the binding site. The model of interaction is then tested and further developed using a series of previously-synthesized dimensional analogs of xanthine and hypoxanthine. The results confirm that the correct positioning of the carbonyl group is essential if a productive interaction with XO is to be achieved and allow us to map the dimensions of the active site starting from the superimposition of the physiol. substrates. Two hypotheses regarding the amino acid residues interacting with the important carbonyl oxygen of the substrates are then put forward on the basis of spectroscopic and biochem. evidence: they are postulated to be one lysine or one protonated glutamic acid residue. To unify the binding of substrates and inhibitors, the model is extended to the inhibitors of XO by superimposing the most interesting inhibitors developed by Robins on xanthine and hypoxanthine. This allows us to define the most suitable location of the Ph rings of these inhibitors with respect to the superimposition of the substrates. Intriguingly, the superimpositions of the most active inhibitors are consistent with a unique location of their Ph rings, even though they are in different positions on the purine ring. Finally, the flavone, which is a potent inhibitor of XO and is currently under investigation by the authors, is accounted for by these findings and successfully included in the model. This model incorporates many important insights into XO and can be of general interest. Moreover, it represents a clear-cut alternative to a previous model developed by Robins on the basis of the coordination of substrates and inhibitors to molybdenum.

IT 53449-18-6
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(relative stabilities of tautomeric forms; model of interaction of substrates and inhibitors with xanthine oxidase)

RN 53449-18-6 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:102094 HCAPLUS

DOCUMENT NUMBER: 126:199575

TITLE: Tricyclic substituted hexahydrobenz[e]isoindole alpha-1 adrenergic antagonists

INVENTOR(S): Meyer, Michael D.; Altenbach, Robert J.; Basha, Fatima Z.; Carroll, William A.; Drizin, Irene; Elmore, Steven W.; Kerwin, James F., Jr.; Lebold, Suzanne A.; Lee, Edmund L.; Sippy, Kevin B.; Tietje, Karin R.; Wendt, Michael D.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: U.S., 73 pp., Cont.-in-part of U.S. Ser. No. 379,414, abandoned.
CODEN: USXXAM

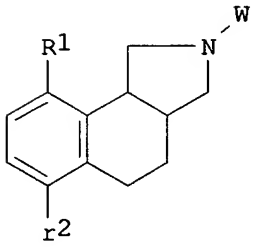
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5597823	A	19970128	US 1995-463528	19950605
IL 116405	A	20010913	IL 1995-116405	19951215
CA 2211212	A1	19960801	CA 1996-2211212	19960111
WO 9622992	A1	19960801	WO 1996-US72	19960111
W: AU, CA, JP, KR, MX				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9647457	A	19960814	AU 1996-47457	19960111
AU 705283	B2	19990520		
EP 808318	A1	19971126	EP 1996-903340	19960111
EP 808318	B1	20000628		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 194141	T	20000715	AT 1996-903340	19960111
ES 2149451	T3	20001101	ES 1996-903340	19960111
PT 808318	T	20001229	PT 1996-903340	19960111
JP 2001504797	T	20010410	JP 1996-522867	19960111
GR 3034485	T3	20001229	GR 2000-402174	20000926
PRIORITY APPLN. INFO.:			US 1995-379414 B2	19950127
			US 1995-463528 A	19950605
			WO 1996-US72 W	19960111

OTHER SOURCE(S): MARPAT 126:199575
GI



I

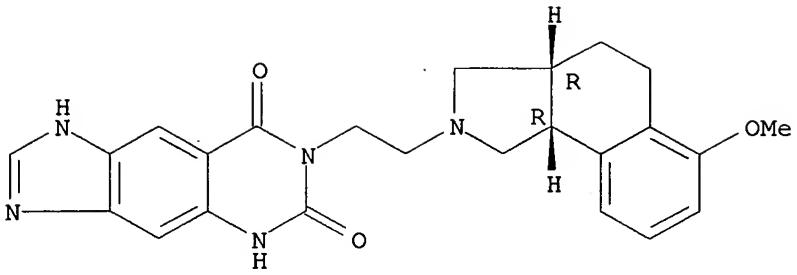
AB I (W = tricyclic heterocyclic ring system, e. g. pyrazinothienopyrimidinediones, pyridofuropyrimidinediones, pyrazinothienopyrimidinediones; n = 2-6; R1 and R2 = H, alkoxy, hydroxy, alkyl, halo, carboxy, alkoxycarbonyl) and their pharmaceutically acceptable salts were prepared I are α-1 adrenergic antagonists and useful in the treatment of BPH (benign prostrate hyperplasia). α-1 Antagonist compns. and a method for antagonizing α-1 receptors and treating BPH are also disclosed.

IT 181281-62-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation as alpha-1 adrenergic antagonists in treatment of benign prostrate hyperplasia)

RN 181281-62-9 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 7-[2-(1,3,3a,4,5,9b-hexahydro-6-methoxy-2H-benz[e]isoindol-2-yl)ethyl]-, dihydrochloride, (3aR-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L4 ANSWER 25 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:721779 HCAPLUS
DOCUMENT NUMBER: 126:8131
TITLE: Preparation of 4-aminoimidazo[5,4-g]quinazolines as inhibitors of tyrosine kinase-mediated signal transduction.
INVENTOR(S): Himmelsbach, Frank; Dahmann, Georg; Von, Rueden Thomas; Metz, Thomas
PATENT ASSIGNEE(S): Karl Thomae Gmbh, Germany
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629331	A1	19960926	WO 1996-EP1082	19960314
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19510019	A1	19960926	DE 1995-19510019	19950320
DE 19600785	A1	19970717	DE 1996-19600785	19960111
AU 9651081	A	19961008	AU 1996-51081	19960314
PRIORITY APPLN. INFO.:			DE 1995-19510019 A	19950320
			DE 1996-19600785 A	19960111
			WO 1996-EP1082 W	19960314

OTHER SOURCE(S): MARPAT 126:8131
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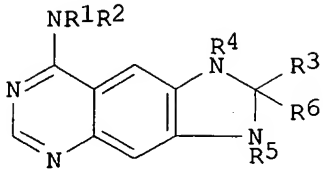

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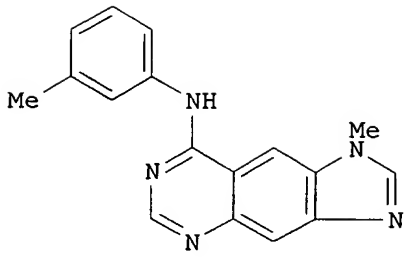


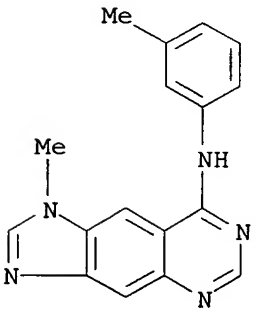
II

AB Title compds. [I; R1 = H, Me; R2 = 2-naphthyl, 1,2,3,4-tetrahydro-6-naphthyl, 5-indanyl, (substituted) Ph; R3 = H, OH, SH, Cl, amino, CO2H, (substituted) alkyl, alkoxy, aminocarbonyl, morpholino, pyrrolidinyl, benzoylamino, tetrahydrofuryl, aryl, etc.; R4 = (substituted) alkyl, cycloalkyl, alkenyl, alkynyl; R5R6 = bond; R3R4 or R3R5 = (alkyl-substituted) (heteroatom-interrupted) alkylene; R4R6, R5R6 = bond], were prepared Thus, 6-methyl-4-methylthioimidazo[5,4-g]quinazoline (preparation given) and m-toluidine were heated at 170° for 2 h to give title compound (II). II inhibited EGF-dependent proliferation of F/L-HERc cells with IC50 = 0.02 μM.

IT 182204-63-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-aminoimidazo[5,4-g]quinazolines as inhibitors of tyrosine kinase-mediated signal transduction)

RN 182204-63-3 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazolin-8-amine, 1-methyl-N-(3-methylphenyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 26 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:664611 HCAPLUS

DOCUMENT NUMBER: 125:301014

TITLE: Preparation of imidazoquinazoline derivatives as cGMP phosphodiesterase inhibitors

INVENTOR(S): Onoda, Yasuo; Sasaki, Shin-ichi; Machii, Daisuke; Takai, Haruki; Ohno, Tetsuji; Yamada, Koji; Ichimura, Michio; Kase, Hiroshi

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan

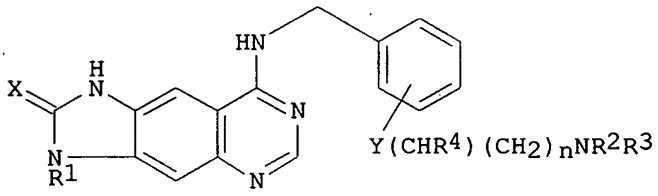
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9626940	A1	19960906	WO 1996-JP497	19960301
W: AU, CA, CN, HU, JP, KR, MX, NO, NZ, PL, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2189355	A1	19960906	CA 1996-2189355	19960301
AU 9648443	A	19960918	AU 1996-48443	19960301
EP 758653	A1	19970219	EP 1996-904302	19960301
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5698560	A	19971216	US 1996-727598	19961023
PRIORITY APPLN. INFO.:			JP 1995-41606 A	19950301
			WO 1996-JP497 W	19960301

OTHER SOURCE(S): MARPAT 125:301014
GI



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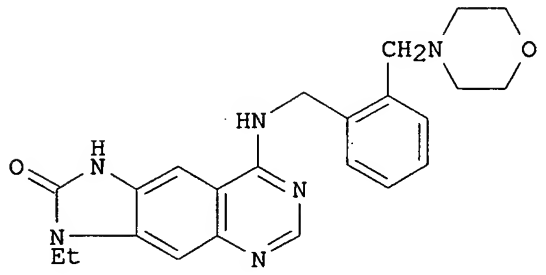


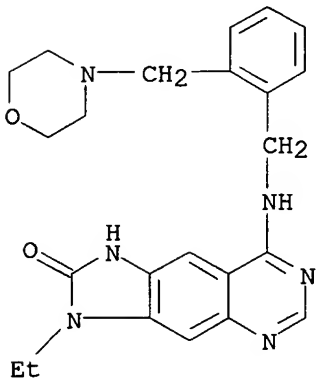
II

AB The title compds. I [R1 represents hydrogen, optionally substituted lower alkyl, etc.; R2 and R3 are the same or different and each represents hydrogen, optionally substituted lower alkyl, optionally substituted aralkyl, optionally substituted aryl, etc., or R2 and R3 together form an optionally substituted nitrogenous heterocycle; R4 represents hydrogen or optionally substituted lower alkyl; X represents O or S; Y represents a single bond or O; and n is 0, 1, 2 or 3] are prepared The title compound II.2HCl (preparation given) in vitro at 1 nM gave 74% inhibition of cGMP phosphodiesterase.

IT 182962-27-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazoquinazoline derivs. as cGMP phosphodiesterase inhibitors)

RN 182962-27-2 HCAPLUS
CN 2H-Imidazo[4,5-g]quinazolin-2-one, 3-ethyl-1,3-dihydro-8-[[[2-(4-

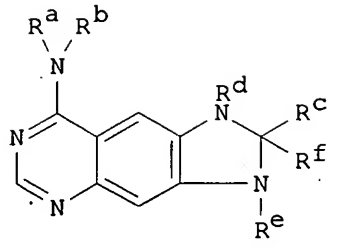
morpholinylmethyl)phenyl]methyl]amino]- (9CI) (CA INDEX NAME)



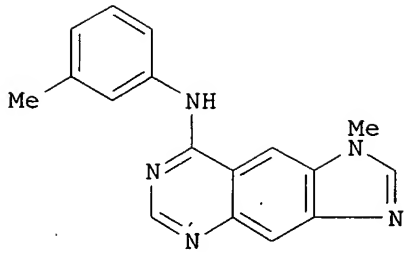
L4 ANSWER 27 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:625525 HCAPLUS
DOCUMENT NUMBER: 125:275902
TITLE: Imidazo[4,5-g]quinazolines, pharmaceuticals containing them, their use as antitumor agents, and process for their preparation.
INVENTOR(S): Himmelsbach, Frank; Dahmann, Georg; Von Rueden, Thomas; Metz, Thomas
PATENT ASSIGNEE(S): Dr. Karl Thomae GmbH, Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
DE 19510019	A1	19960926	DE 1995-19510019		19950320
WO 9629331	A1	19960926	WO 1996-EP1082		19960314
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9651081	A	19961008	AU 1996-51081		19960314
PRIORITY APPLN. INFO.:			DE 1995-19510019	A	19950320
			DE 1996-19600785	A	19960111
			WO 1996-EP1082	W	19960314

OTHER SOURCE(S): MARPAT 125:275902
GI



I



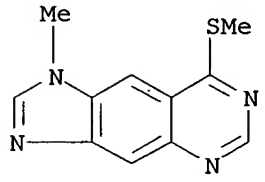
II

AB Title compds. I [Ra = H, Me; Rb = 2-naphthyl, 1,2,3,4-tetrahydro-6-naphthyl, 5-indanyl, (un)substituted Ph; Rc = H, OH, SH, Cl, NH2, CO2H, (un)substituted alkyl, etc.; Rd = (un)substituted alkyl, cycloalkyl, etc.; or RdRf or ReRf = bond; or RcRd or RcRe = alkylene with optional alkyl substitution or heteroatom replacement] and their salts, stereoisomers, and tautomers are claimed. I are inhibitors of signal transduction mediated by epidermal growth factor receptor (EGF-R), and as such are particularly useful for treating tumors and other hyperproliferative diseases. Thus, 8-(methylthio)-1H-imidazo[4,5-g]quinazoline underwent N-methylation using KOCMe3 and MeI in DMF, followed by condensation with m-toluidine at 175°, to give title compound II. The latter inhibited EGF-dependent proliferation of F/L-HERc cells in vitro with an IC50 of 0.020 μM, but inhibited IL-3-dependent proliferation with an IC50 of >1 μM.

IT 174709-19-4P, 1-Methyl-8-(methylthio)-1H-imidazo[4,5-g]quinazoline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of imidazoquinazolines as antitumor agents)

RN 174709-19-4 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline, 1-methyl-8-(methylthio)- (9CI) (CA INDEX NAME)



L4 ANSWER 28 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:580282 HCAPLUS

DOCUMENT NUMBER: 125:221858

TITLE: Preparation of tricyclic substituted benz[e]isoindoles as α1 adrenergic antagonists

INVENTOR(S): Meyer, Michael D.; Altenbach, Robert J.; Basha, Fatima Z.; Carroll, William A.; Drizin, Irene; Kerwin, James F., Jr.; Lebold, Suzanne A.; Lee, Edmund L.; Elmore, Steven W.; et al.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622992	A1	19960801	WO 1996-US72	19960111
W: AU, CA, JP, KR, MX				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5597823	A	19970128	US 1995-463528	19950605
AU 9647457	A	19960814	AU 1996-47457	19960111
AU 705283	B2	19990520		
EP 808318	A1	19971126	EP 1996-903340	19960111
EP 808318	B1	20000628		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AT 194141	T	20000715	AT 1996-903340	19960111
JP 2001504797	T	20010410	JP 1996-522867	19960111
GR 3034485	T3	20001229	GR 2000-402174	20000926
PRIORITY APPLN. INFO.:			US 1995-379414 A	19950127
			US 1995-463528 A	19950605
			WO 1996-US72 W	19960111

OTHER SOURCE(S): MARPAT 125:221858
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

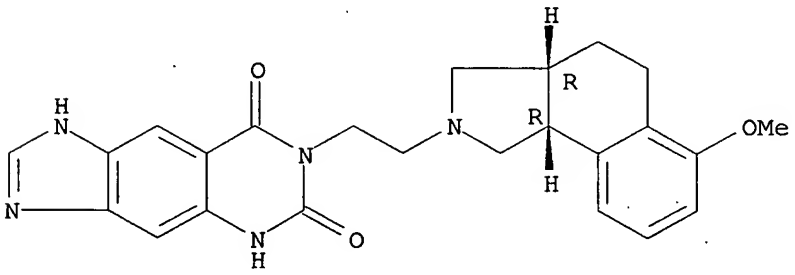
AB The title compds. [I; R1, R2 = H, alkoxy, OH, etc.; W = tricyclic heterocyclic ring system; n = 2-6] and their salts, useful in the treatment of benign prostatic hypertrophy (BPH), were prepared Thus, reaction of urea II with benz[e]isoindole III in the presence of (iPr)2NEt in DMSO afforded the desired product cis-IV.HCl which showed pA2 of 8.37 for inhibition of phenylepherine(PE)-induced contraction of rat vas.

IT 181281-62-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic substituted benz[e]isoindoles as α1 adrenergic antagonists)

RN 181281-62-9 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 7-[2-(1,3,3a,4,5,9b-hexahydro-6-methoxy-2H-benz[e]isoindol-2-yl)ethyl]-, dihydrochloride, (3aR-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

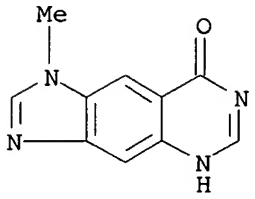


●2 HCl

L4 ANSWER 29 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:536936 HCAPLUS
Correction of: 1996:73866
DOCUMENT NUMBER: 125:195598
Correction of: 124:232395
TITLE: Tyrosine kinase inhibitors. 9. Synthesis and evaluation of fused tricyclic quinazoline analogs as ATP site inhibitors of the tyrosine kinase activity of the epidermal growth factor receptor
AUTHOR(S): Rewcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.
CORPORATE SOURCE: Sch. Med., Univ. Auckland, Auckland, 92019, N. Z.
SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 918-928
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

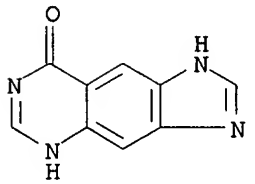
IT 171179-64-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate in preparation of imidazoquinazolines as tyrosine kinase inhibitors)
RN 171179-64-9 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro-1-methyl- (9CI) (CA INDEX NAME)



L4 ANSWER 30 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:109105 HCAPLUS
DOCUMENT NUMBER: 124:249637
TITLE: A survey of nonxanthine derivatives as adenosine receptor ligands
AUTHOR(S): Siddiqi, Suhaib M.; Ji, Xiao-duo; Melman, Neli; Olah, Mark E.; Jain, Rahul; Evans, Patricia; Glashofer, Marc; Padgett, William L.; Cohen, Louis A.; et al.
CORPORATE SOURCE: Molecular Recognition Section, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Nucleosides & Nucleotides (1996), 15(1-3), 693-717
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The binding affinities at rat A1, A2a, and A3 adenosine receptors of a wide range of heterocyclic derivs. have been determined Mono-, bi-, tricyclic and macrocyclic compds. were screened in binding assays, using either [3H]PIA or [3H]CGS 21680 in rat brain membranes or [125I]AB-MECA in CHO cells stably transfected with rat A3 receptors. Several new classes of adenosine antagonists (e.g. 5-oxoimidazopyrimidines and a pyrazoloquinazoline) were identified. Various sulfonylpiperazines, 11-hydroxytetrahydrocarbazolenine, 4H-pyrido[1,2-a]pyrimidinone, folic acid, and cytochalasin H and J bound to A3 receptors selectively. Moreover, cytochalasin A, which bound to A1 adenosine receptors with Ki value of 1.9 μM, inhibited adenylyl cyclase in rat adipocytes, but not via reversible A1 receptor binding.

IT 53449-18-6, lin-Benzohypoxanthine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonxanthine derivs. as adenosine receptor ligands)
RN 53449-18-6 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 31 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:73866 HCAPLUS
DOCUMENT NUMBER: 124:232395
TITLE: Tyrosine Kinase Inhibitors. 9. Synthesis and

Evaluation of Fused Tricyclic Quinazoline Analogs as ATP Site Inhibitors of the Tyrosine Kinase Activity of the Epidermal Growth Factor Receptor

AUTHOR(S): Rewcastle, Gordon W.; Palmer, Brian D.; Bridges, Alexander J.; Showalter, H. D. Hollis; Sun, Li; Nelson, James; McMichael, Amy; Kraker, Alan J.; Fry, David W.; Denny, William A.

CORPORATE SOURCE: School of Medicine, University of Auckland, Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 918-28
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

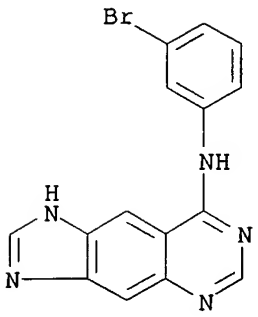
LANGUAGE: English

AB Following the discovery of 4-[(3-bromophenyl)amino]-6,7-dimethoxyquinazoline (PD 153035) as an extremely potent (IC50 0.025 nM) inhibitor of the tyrosine kinase activity of the epidermal growth factor receptor (EGFR), several fused tricyclic quinazoline analogs have been prepared and evaluated for their ability to inhibit the enzyme. The most potent compound was a linear imidazo[4,5-g]quinazoline, which exhibited an IC50 of 0.008 nM for inhibition of phosphorylation of a fragment of phospholipase C-γ1 as substrate. While N-Me analogs of linear imidazo[4,5-g]quinazolines showed similar potency, analogous N-[2-(dimethylamino)ethyl] derivs. were less effective. The next most potent compds. were linear pyrazoloquinazoline analogs (IC50s 0.34 and 0.44 nM) and a pyrroloquinazoline analog (IC50 0.44 nM), while several other linear tricyclic ring systems of similar geometry to linear imidazo[4,5-g]quinazolines (triazolo-, thiazolo-, and pyrazinoquinazolines) were less effective. In the imidazo[4,5-g]quinazoline and pyrroloquinazoline series, the corresponding angular isomers were also much less effective than the linear ones. These results are consistent with structure-activity relationship studies previously developed for the 4-[(3-bromophenyl)amino]quinazolines, which suggested that small electron-donating substituents at the 6- and 7-positions were desirable for high potency. Cellular studies of a linear imidazo[4,5-g]quinazoline, i.e., N-(3-bromophenyl)-1H-imidazo[4,5-g]quinazolin-8-amine, show that it can enter cells and rapidly and very selectively shut down EGF-stimulated signal transmission by binding competitively at the ATP site of the EGFR.

IT 171179-32-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of imidazo[4,5-g]quinazoline analogs as tyrosine kinase inhibitors)

RN 171179-32-1 HCAPLUS

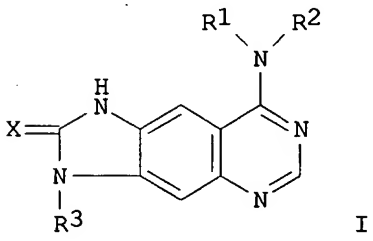
CN 1H-Imidazo[4,5-g]quinazolin-8-amine, N-(3-bromophenyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 32 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:846525 HCAPLUS
DOCUMENT NUMBER: 123:256749
TITLE: Preparation of imidazoquinazoline derivatives having cyclic guanosine 3',5'-monophosphate (cGMP)-specific phosphoesterase inhibitor activity
INVENTOR(S): Machii, Daisuke; Matsuno, Kenji; Kinoshita, Iwao; Nomoto, Yuji; Takai, Haruki; Ohno, Tetuji; Nagashima, Ken; Ishikawa, Tomoko; Yamada, Koji; et al.
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9506648	A1	19950309	WO 1994-JP1456	19940902
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2148082	A1	19950309	CA 1994-2148082	19940902
EP 668280	A1	19950823	EP 1994-925621	19940902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5661147	A	19970826	US 1995-424274	19950426
PRIORITY APPLN. INFO.:			JP 1993-219595 A	19930903
			WO 1994-JP1456 W	19940902

OTHER SOURCE(S): MARPAT 123:256749
GI



I

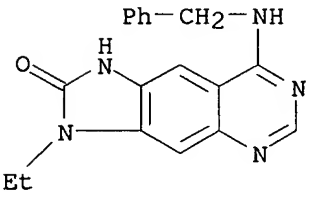
AB Imidazoquinazoline derivs. represented by formula [I; R1, R2 = H, (un)substituted lower alkyl, cycloalkyl, bicycloalkyl, (un)substituted benzocycloalkyl, lower alkenyl, (un)substituted aryl, ring-(un)substituted

aromatic heterocyclylalkyl, aromatic heterocyclyl, or aralkyl; or NR1R2 = (un)substituted heterocyclyl; R3 = H, lower alkyl, cycloalkyl, lower alkenyl, ring-(un)substituted aryl, aromatic heterocyclylalkyl, aromatic heterocyclyl, or aralkyl presents hydrogen, lower alkyl, cycloalkyl alkenyl; X = O, S] or pharmacol. acceptable salts thereof are prepared These compds. have a potent and selective cGMP-specific PDE inhibitor activity and are useful for treating or mitigating cardiovascular diseases such as thrombosis, angina pectoris, hypertension and arteriosclerosis, asthma and so forth. Thus, 4-benzylamino-7-ethylamino-6-nitroquinazoline (preparation given) was hydrogenated in the presence of 10% Pd-C in DMF at room temperature for 5 h and 50° for 1 h to give 95.2% 6-amino-4-benzylamino-7-ethylamioquinazoline which was cyclocondensed with N,N-carbonyldiimidazole in DMF at 100° for 3.5 h to give 47.3% I (X = O, R1 = CH2Ph, R2 = H, R3 = Et). I (X = S, R1 = CH2Ph, R2 = H, R3 = Et) in vitro showed IC50 of 0.18,1,100, and >10,000 nM against PDE V (cGMP-specific phosphoesterase), PDE III (cGMP-inhibited cAMP-specific phosphoesterase), and PDE IV (cAMP-specific phosphoesterase), resp., and at 30 μg/kg i.v. in vivo lowered the median blood pressure by maximum 51.2% in guinea pigs.

IT 168760-22-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazoquinazoline derivs. as cGMP-specific phosphoesterase inhibitors)

RN 168760-22-3 HCAPLUS

CN 2H-Imidazo[4,5-g]quinazolin-2-one, 3-ethyl-1,3-dihydro-8-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)



L4 ANSWER 33 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:758310 HCAPLUS

DOCUMENT NUMBER: 123:192053

TITLE: P-glycoprotein is stably inhibited by vanadate-induced trapping of nucleotide at a single catalytic site

AUTHOR(S): Urbatsch, Ina L.; Sankaran, Banumathi; Weber, Joachim; Senior, Alan E.

CORPORATE SOURCE: Med. Cent., Univ. Rochester, Rochester, NY, 14642, USA

SOURCE: Journal of Biological Chemistry (1995), 270(33), 19383-90
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Bio logy

DOCUMENT TYPE: Journal

LANGUAGE: English

AB P-glycoprotein (Pgp or multidrug-resistance protein) shows drug-stimulated ATPase activity. The catalytic sites are known to be of low affinity and specificity for nucleotides. From the sequence, two nucleotide sites are predicted per Pgp mol. Using plasma membranes from a multidrug-resistant Chinese hamster ovary cell line, which are highly enriched in Pgp, the authors show that vanadate-induced trapping of nucleotide at a single catalytic site produces stably inhibited Pgp, with t1/2 for reactivation

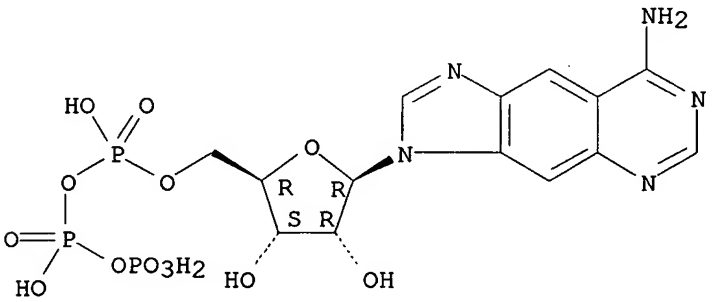
of ATPase activity of 84 min at 37° and >30 h at 4°. Reactivation of ATPase correlated with release of trapped nucleotide. Concns. of MgATP and MgADP required to produce 50% inhibition were 9 and 15 μM, resp., thus the apparent affinity for nucleotide is greatly increased by vanadate-trapping. The trapped nucleotide species was ADP. Divalent cation was required, with magnesium, manganese, and cobalt all effective; cobalt yielded a very stable inhibited species, t1/2 at 37° = 18 h. No photocleavage of Pgp was observed after vanadate trapping with MgATP, nor was UV-induced photolabeling of Pgp by trapped adenine nucleotide observed Vanadate-trapping with 8-azido-ATP followed by UV irradiation caused permanent inactivation and specific labeling of Pgp. Vanadate-induced inhibition was also shown with pure, reconstituted Pgp, with similar characteristics to those in plasma membranes. Vanadate trapping overcomes tech. difficulties posed by lack of high affinity nucleotide-binding site(s) or a covalent enzyme-phosphate catalytic intermediate in Pgp. The finding that vanadate trapping of nucleotide at just one site/Pgp is sufficient to give full inhibition of ATPase activity shows that the two predicted nucleotide sites can not function independently as catalytic sites.

IT 61925-58-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(P-glycoprotein is stably inhibited by vanadate-induced trapping of nucleotide at a single catalytic site)

RN 61925-58-4 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 34 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:675778 HCAPLUS

DOCUMENT NUMBER: 121:275778

TITLE: lin-Benzo-ATP and -ADP: versatile fluorescent probes for spectroscopic and biochemical studies

AUTHOR(S): Grell, E.; Lewitzki, E.; Bremer, C.; Kramer-Schmitt, S.; Weber, J.; Senior, A. E.

CORPORATE SOURCE: Max-Planck-Inst. Biophys., Frankfurt, 60596, Germany

SOURCE: Journal of Fluorescence (1994), 4(3), 247-50
CODEN: JOFLEN; ISSN: 1053-0509

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lin-Benzo-adenine nucleotides can act not only as probes for fluorescence studies but also as structural active site probes for enzymes. To understand the basic properties of lin-benzo-ATP and -ADP, protolysis and Mg2+ and Ca2+ binding are investigated between pH 6.2 and pH 8.5 by

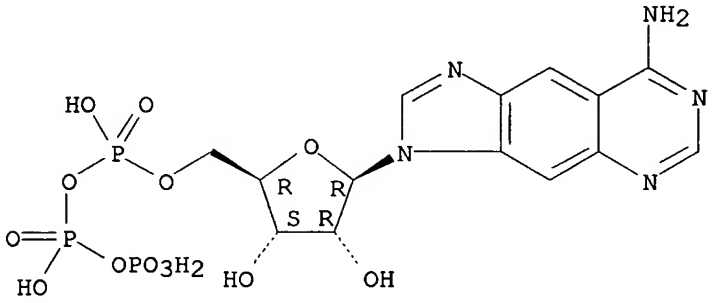
spectrophotometric and spectrofluorometric titrns. Based on a reaction model, a set of equilibrium consts. is determined which is consistent with all available exptl. results. The pK values of the Mg2+ and Ca2+ complex of lin-benzo-ATP in the chosen medium are 4.6 and 4.1, resp., and those for the corresponding diphosphate are 3.1 and 2.8, resp. Fluorescence and absorption spectra are reported.

IT 61925-58-4, Lin-Benzo-ATP
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fluorescent probes for spectroscopic and biochem. studies)

RN 61925-58-4 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 35 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:186038 HCAPLUS

DOCUMENT NUMBER: 120:186038

TITLE: Tryptophan-free Escherichia coli F1-ATPase

AUTHOR(S): Wilke-Mounts, Susan; Weber, Joachim; Grell, Ernst; Senior, Alan E.

CORPORATE SOURCE: Med. Cent., Univ. Rochester, Rochester, NY, 14642, USA

SOURCE: Archives of Biochemistry and Biophysics (1994), 309(2), 363-8
CODEN: ABBIA4; ISSN: 0003-9861

DOCUMENT TYPE: Journal

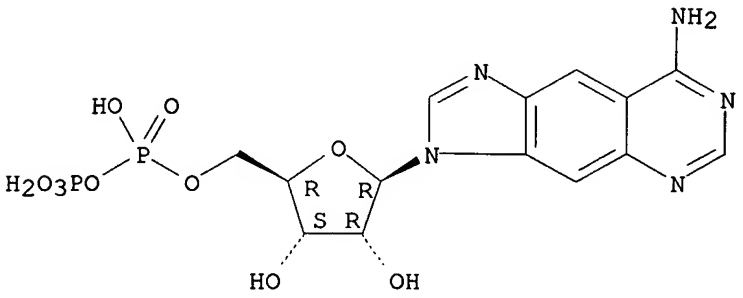
LANGUAGE: English

AB The authors have engineered a mutant form of Escherichia coli F1-ATPase which is tryptophan-free and contains five mutations, namely δW28L/αW513F/γW108Y/γW206Y/βW107F. A strain carrying all five mutations grew normally by oxidative phosphorylation. Purified mutant F1-ATPase showed Vmax and Km both 65% higher than wild-type, resulting in kcat/Km the same as wild-type. The pH dependence of ATPase activity in the mutant enzyme was very similar to that in wild-type. Catalytic-site nucleotide-binding characteristics were measured using the analog lin-benzo-ADP and sensitivity to inhibitors was tested using dicyclohexylcarbodiimide, azide and aurovertin. The mutant enzyme was very similar to wild-type in each of these characteristics. The fluorescence spectrum of the mutant enzyme confirmed the absence of tryptophan. The authors have therefore established that it is possible to generate a tryptophan-free enzyme which retains normal catalytic function, oligomeric stability and in vivo assembly.

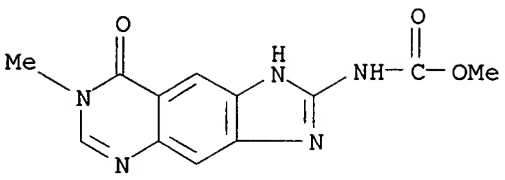
IT 61925-59-5, lin-Benzo-adp
RL: BIOL (Biological study)
(ATPase tryptophan-free form of Escherichia coli interaction with, engineered enzyme catalytic sites in relation to)

RN 61925-59-5 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

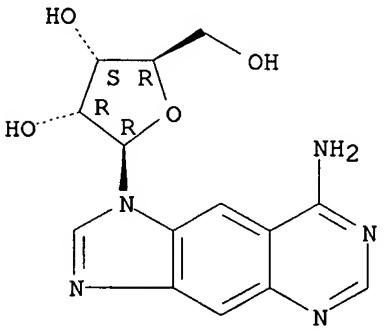


L4 ANSWER 36 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:124172 HCAPLUS
DOCUMENT NUMBER: 120:124172
TITLE: Segregation of activity profile in benzimidazoles: effect of spacers at 5(6)-position of methyl benzimidazole-2-carbamates
AUTHOR(S): Agarwal, Shiv K.; Sharma, Satyavan; Bhaduri, A. P.
CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226001, India
SOURCE: Zeitschrift fuer Naturforschung, C: Journal of Biosciences (1993), 48(11-12), 829-38
CODEN: ZNCBDA; ISSN: 0341-0382
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The design and synthesis of a series of Me 5(6)-substituted benzimidazole-2-carbamates as potential anthelmintics are described. A rational anal. of the structural parameters which segregate the activity of resulting benzimidazole-2-carbamates against enteric and tissue dwelling helminths is presented. The influence of single and multiple spacers, which link the pharmacophores at 5(6)-position of benzimidazole-2-carbamate, on the activity against Ancylostoma ceylanicum (hookworm), Syphacia obvelata (pinworm), Hymenolepis nana (tapeworm) Litomosoides carinii and Acanthocheilonema viteae (filarial worm) has been presented. This anal. indicates that for activity against intestinal helminth the presence of one spacer holding the pharmacophore approx. 3 Å apart from the parent nucleus is usually preferred. While for activity against tissue dwelling parasite, the repetition of the benzimidazole-2-carbamate nucleus joined together through the 5,5'-position with one spacer kept apart by distance of 3 Å unit is usually desired.
IT 81946-14-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anthelmintic activity of, structure-activity relations in)
RN 81946-14-7 HCAPLUS
CN Carbamic acid, (7,8-dihydro-7-methyl-8-oxo-1H-imidazo[4,5-g]quinazolin-2-yl)-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 37 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:506636 HCAPLUS
DOCUMENT NUMBER: 117:106636
TITLE: Molecular biological characterization of ligand-gated ion channel/receptors in Lymnaea
AUTHOR(S): Vreugdenhil, Erno; Harvey, Robert J.; Van Marle, Andre; Barnard, Erich A.; Darlison, Mark G.
CORPORATE SOURCE: Fac. Chem., Vrije Univ., Amsterdam, 1081 HV, Neth.
SOURCE: Verhandelingen - Koninklijke Nederlandse Akademie van Wetenschappen, Afdeling Natuurkunde, Tweede Reeks (1991), 88(Molluscan Neurobiol.), 353-8
CODEN: VNAWAG; ISSN: 0373-465X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ligand-gated ion-channel receptors play an important role in signal transduction in the central nervous systems of vertebrate and invertebrate species. Based on their structural and sequence similarities, subunits of these receptors have been proposed to be members of a superfamily. Several genomic and cDNA clones, that encoded putative γ-aminobutyric acid receptor and nicotinic acetylcholine receptor subunits, were isolated from the freshwater snail L. stagnalis, and characterized. Some of the predicted features of these polypeptides will be discussed.
IT 60189-88-0
RL: BIOL (Biological study)
(receptor for, of Lymnaea stagnalis, mol. biol. characterization of)
RN 60189-88-0 HCAPLUS
CN 1H-Imidazo[4,5-g]quinazolin-8-amine, 1-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



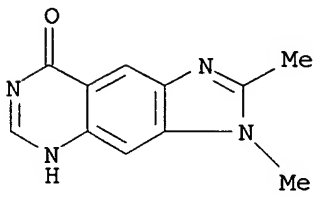
L4 ANSWER 38 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:485818 HCAPLUS
DOCUMENT NUMBER: 117:85818
TITLE: Modified purines as mechanistic probes of substrates

oxidation by xanthine oxidase
AUTHOR(S): Lee, Chang Hee; Han, In Sup
CORPORATE SOURCE: Dep. Chem., Kangweon Natl. Univ., Chuncheon, 200-701, S. Korea
SOURCE: Journal of the Korean Chemical Society (1992), 36(2), 335-7
CODEN: JKCSEZ; ISSN: 0418-2472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Substrate specificity of xanthine oxidase (I) 4-substituted imidazo[4,5-g]quinazoline derivs. was examined with regard to I reaction mechanism. The Hammet plot for the substrates oxidation is reported. Kinetic isotope effect obtained from the 4-bromo and 4-H substituents is also described. It is concluded that oxidation involved nucleophile transfer to the C(6) center in concert with hydride (or its equivalent) transfer to the Mo center. Thus nucleophile increases the electron d. in the substrates and thereby facilitate the hydride transfer.

IT 71249-73-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with xanthine oxidase, kinetics of, structure in relation to)

RN 71249-73-5 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 3,5-dihydro-2,3-dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 39 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:467360 HCAPLUS
DOCUMENT NUMBER: 115:67360
TITLE: Structure-activity relationship of ligands of human plasma adenosine deaminase2
AUTHOR(S): Niedzwicki, John G.; Abernethy, Darrell R.
CORPORATE SOURCE: Div. Clin. Pharmacol., Brown Univ., Providence, RI, USA
SOURCE: Biochemical Pharmacology (1991), 41(11), 1615-24
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

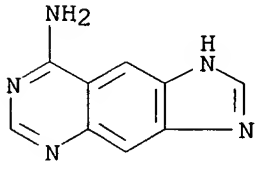
AB Diethylaminoethyl-cellulose chromatog. was used to sep. the two isoenzymes of adenosine deaminase (EC 3.5.4.4), adenosine deaminase1 (ADA1) and adenosine deaminase2 (ADA2), in human plasma. One hundred and fifteen purine base, nucleoside, and nucleotide analogs were tested as inhibitors of this partially purified preparation of ADA2. Coformycin and 2'-deoxycoformycin were by far the most potent inhibitors of this isoenzyme (apparent Ki values 20 and 19 nM, resp.). ADA2 was also inhibited by nebularine (apparent Ki 1.5 mM) but was resistant to the potent ADA1 inhibitor (+)-erytho-9(2-S-hydroxy-3-R-nonyl)adenine. α-D-Adenosine also inhibited ADA2, as did several halogenated purine and adenine base analogs. Structural requirements for the binding of purine analogs to ADA2 are presented which provide a general basis for the design of specific inhibitors of ADA2. Such inhibitors may be useful in

studies designed to provide an understanding of the physiol. role of ADA2 both in the normal state and in diseases such as human immunodeficiency virus-1 infection where levels in plasma are increased markedly.

IT 53449-12-0, lin-Benzoadenine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(adenosine deaminase isoenzyme 2 of blood plasma of human inhibition by, structure in relation to)

RN 53449-12-0 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine (CA INDEX NAME)



L4 ANSWER 40 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:43445 HCAPLUS

DOCUMENT NUMBER: 114:43445

TITLE: Regioselective synthesis of imidazo[4,5-g]quinazoline quinone nucleosides and quinazoline amino nucleosides. Studies of their xanthine oxidase and purine nucleoside phosphorylase substrate activity

AUTHOR(S): Dempcy, Robert O'Hara; Skibo, Edward B.

CORPORATE SOURCE: Dep. Chem., Arizona State Univ., Tempe, AZ, 85287-1604, USA

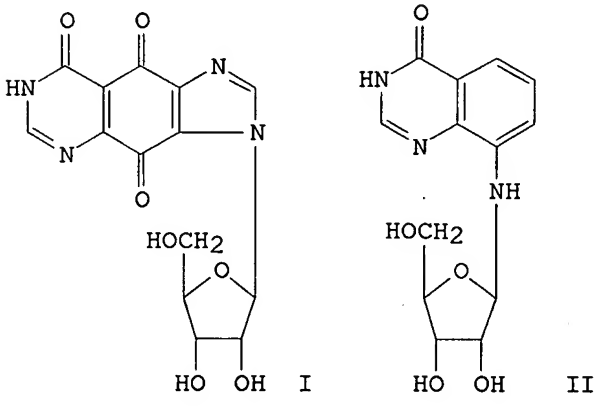
SOURCE: Journal of Organic Chemistry (1991), 56(2), 776-85
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 114:43445

GI



I

II

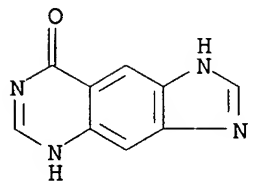
AB The regioselective synthesis of ribofuranosylimidazoquinazolines I and II was carried out in conjunction with the design of reductive alkylating nucleosides and new purine nucleoside mimics, resp. The preparation of I was

carried out by regioselective ribosylation of 4-nitroimidazo[4,5-g]quinazolin-8(3H,7H)-one (III) followed by nitro group reduction, Fremy oxidation, and deacetylation. Regiocontrol of ribosylation has steric origins: the 4-nitro group of III directs silylation to the N(1) position, which results in ribosylation exclusively at the N(3) position under Vorbruggen reaction conditions. Regiocontrol during the preparation of II was possible by generating a stabilized ribofuranosyl carbocation, which selectively reacts with the amine group of the base. Nucleoside I is a purine-like quinone by virtue of its oxidation by xanthine oxidase. The potential inosine mimic II does not undergo phosphorolysis by purine nucleoside phosphorylase (PNPase), but the base 8-aminoquinazolin-4(3H)-one does bind to the PNPase active site as tightly as hypoxanthine. Factors which contribute to this binding behavior are discussed.

IT 53449-18-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(nitration of, in synthesis of nucleosides)

RN 53449-18-6 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 41 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:511561 HCAPLUS

DOCUMENT NUMBER: 113:111561

TITLE: Differentiation of the nucleotide-binding sites on nucleotide-depleted mitochondrial F1-ATPase by means of a fluorescent ADP analog

AUTHOR(S): Weber, Joachim; Schmitt, Sabine; Grell, Ernst; Schaefer, Guenter

CORPORATE SOURCE: Inst. Biochem., Med. Univ. Luebeck, Luebeck, D-2400/1, Germany

SOURCE: Journal of Biological Chemistry (1990), 265(19), 10884-92
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The interaction of the fluorescent ADP analog lin-benzo-ADP (containing a linearly extended version of adenine, in which a benzene ring is inserted between pyrimidine and imidazole ring) with nucleotide-depleted mitochondrial F1 was investigated. It was found that lin-benzo-ADP is able to occupy all six nucleotide-binding sites present on the enzyme. Two sites exhibit a very high affinity for the analog (dissociation constant, Kd, ≤ 10 nM) and bind it rapidly (association rate constant, k+1, about 1·106M-1 s-1). A third site shows a lower affinity for the analog (Kd = 1-2 μM) and is occupied relatively fast (k+1 ≈ 104M-1 s-1). Binding of lin-benzo-ADP to these three sites is prevented not only in the presence of excess ADP and ATP, but also by IDP and ITP, thus indicating that these sites are the catalytic ones. As it will be discussed, this conclusion is further corroborated by the finding that release of the analog from the two high affinity sites can be promoted by binding of nucleoside di- and triphosphates to the third site. The remaining three sites were found to bind lin-benzo-ADP with identical

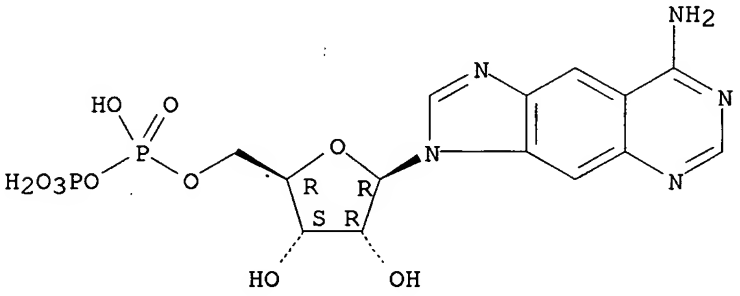
affinity (Kd = 1-2 μM) and with a rather low association rate (k+1 = 300-600M-1 s-1). Binding of the analog to them is only prevented by ADP and ATP, but not by IDP and ITP, which confirms that these sites are the noncatalytic ones. The analog could be displaced by excess ADP also from these sites; however, in contrast to the catalytic sites, no promotive effect was observed here. The obvious changes in the nucleotide binding behavior of the noncatalytic sites after depletion of endogenous nucleotides will be discussed.

IT 61925-59-5
RL: PROC (Process)
(ATPase of mitochondria binding of, in studies of nucleotide-binding sites)

RN 61925-59-5 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 42 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:454872 HCAPLUS

DOCUMENT NUMBER: 113:54872

TITLE: The basal magnesium-dependent ATPase activity is not part of the hydrogen ion-potassium-transporting ATPase reaction cycle

AUTHOR(S): Van der Hijden, Harry T. W. M.; Kramer-Schmitt, Sabine; Grell, Ernst; De Pont, Jan Joep H. H. M.

CORPORATE SOURCE: Dep. Biochem., Univ. Nijmegen, Nijmegen, 6500 HB, Neth.

SOURCE: Biochemical Journal (1990), 267(3), 565-72
CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purified gastric (H+ + K+)-ATPase from parietal cells always contains a certain amount of basal Mg2+-ATPase activity. lin-Benzo-ATP (I) was used in the present study to elucidate the possible role of the basal Mg2+-ATPase activity in the gastric (H+ + K+)-ATPase preparation With I, the enzyme could be phosphorylated such that a conventional phosphoenzyme intermediate was formed. The rate of the phosphorylation reaction, however, was so low that this reaction with subsequent dephosphorylation could not account for the much higher rate of hydrolysis of I by the enzyme. This apparent kinetic discrepancy indicated that I is not a substrate for the (H+ + K+)-ATPase reaction cycle. This idea was further supported by the finding that I was unable to catalyze H+ uptake by gastric mucosa vesicles. The breakdown of I by the (H+ + K+)-ATPase preparation must be due to a hydrolytic activity which is not involved in the ion-transporting reaction cycle of the (H+ + K+)-ATPase itself. Comparison of the basal Mg2+-ATPase activity (with ATP as substrate) with the hydrolytic activity of (H+ + K+)-ATPase using I as substrate and the effect of the inhibitors, omeprazole and SCH

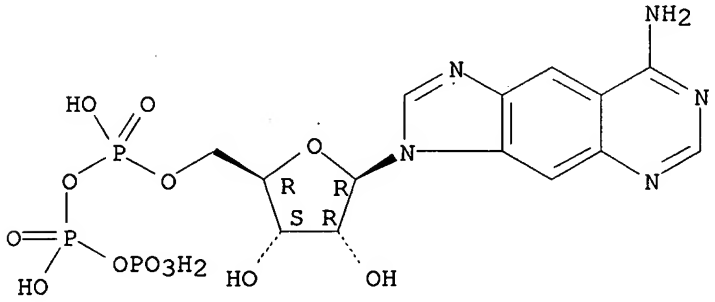
28080, supported the notion that I is not hydrolyzed by the (H+ + K+)-ATPase, but by the basal Mg2+-ATPase, and that the activity of the latter enzyme is not involved in the (H+ + K+)-transporting reaction cycle (according to the Albers-Post formalism) of (H+ + K+)-ATPase.

IT 61925-58-4
RL: BIOL (Biological study)
(ATPase proton-potassium-activated and magnesium-activated activities of stomach differential interactions with)

RN 61925-58-4 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 43 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:212992 HCAPLUS

DOCUMENT NUMBER: 112:212992

TITLE: A quantum chemical study of the enzymic deamination of benzoadenine derivatives. A theoretical model of the interactions occurring between nucleosides and the active site of adenosine deaminase

AUTHOR(S): Orozco, Modesto; Canela, Enric I.; Franco, Rafael

CORPORATE SOURCE: Fac. Quim., Univ. Barcelona, Barcelona, E-08028, Spain

SOURCE: European Journal of Biochemistry (1990), 188(1), 155-63
CODEN: EJBCAI; ISSN: 0014-2956

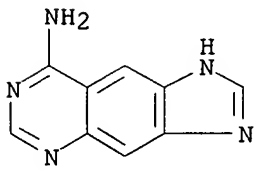
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A theor. study is presented, where, by using both ab initio and semi-empirical methodologies, the properties of benzoadenine derivs. as substrates of adenosine deaminase are discussed. The results suggest that lin-benzoadenine and lin-benzoadenosine can be recognized with an affinity similar to that of adenosine, but only if they are introduced about 0.12 nm deeper inside the active site of the enzyme than the natural substrate adenosine. This fact implies the existence of nonlinear H bonds inside the active site of adenosine deaminase. Ab initio mol. electrostatic potential values suggest that these H bonds can exist, and have stability similar to that of linear H bonds. Finally, the great rate of deamination of lin-benzoadenine, comparable with that of adenosine-despite the absence of the ribose, is explained in the context of the hypothesis that the protonation at the N1 atom is the rate-determining step of the whole deamination reaction.

IT 53449-12-0, lin-Benzoadenine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with adenosine deaminase, quantum chemical study of)

RN 53449-12-0 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine (CA INDEX NAME)



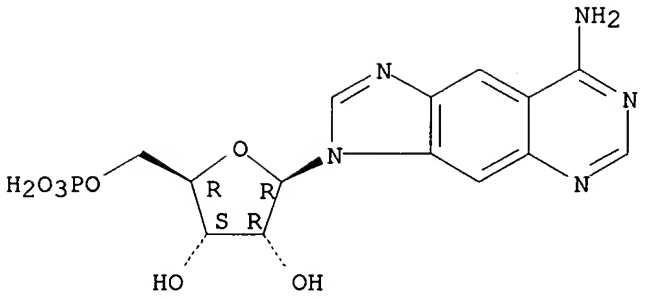
L4 ANSWER 44 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:194412 HCAPLUS
DOCUMENT NUMBER: 112:194412
TITLE: Structural requirements for the binding of AMP to the allosteric site of NAD-specific isocitrate dehydrogenase from bakers' yeast
AUTHOR(S): Gabriel, Jerome L.; Plaut, Gerhard W. E.
CORPORATE SOURCE: Sch. Med., Temple Univ., Philadelphia, PA, 19140, USA
SOURCE: Biochemistry (1990), 29(14), 3528-35
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The specificity of yeast NAD-specific isocitrate dehydrogenase for the structures of the allosteric effector, AMP, was examined with analogs modified in the purine ring, pentosyl group, and 5'-phosphate group. An unsubstituted 6-amino group was essential for activation as was the phosphoryl group at the 5'-position. Activity was retained when an O function of the 5'-phosphoryl was replaced by S or by N (phosphoramidates). 2-NH2-AMP, 2-azido-AMP, and 8-NH2-AMP were active; 8-azido-AMP and 8-Br-AMP were inactive. The configuration or nature of substituents about C-2' and C-3' of the pentosyl portion of AMP was not critical for allosteric activation since AMP analogs containing, e.g., 2',3'-dideoxyribose or the bulky 2',3'-O-(2,4,6-trinitrocyclohexadienylidene) substituent (TNP-AMP) were active. TNP-AMP was bound to the enzyme with fluorescence enhancement and had an S0.5 for activation similar to the S0.5 for AMP. Pos. effector activity was decreased when the pentosyl moiety of AMP was replaced by the 6-membered N-containing morpholine group, indicating that the pentosyl group may be critical as a spacer for the proper geometry of binding to enzyme at the 6-amino and 5'-phosphoryl groups of AMP. A comparison of mol. models of AMP with 8,5'-cycloAMP suggested that the species of AMP required for binding to the enzyme contains the purine and ribose moieties in an anti conformation and positioning of the 5'-phosphate trans with respect to C-4'. This was consistent with the finding that (S)-8,5'-cycloAMP was a potent neg. allosteric modifier (i.e., it increased the Km for isocitrate) whose effect could be reversed competitively by AMP, whereas the R epimer was inactive.

IT 67126-65-2
RL: BIOL (Biological study)
(isocitrate dehydrogenase of yeast response to, structure in relation to)

RN 67126-65-2 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-(5-O-phosphono-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

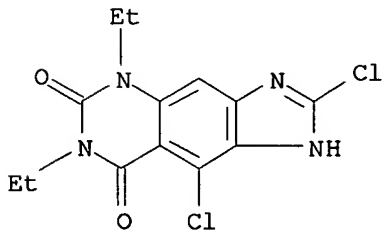
Absolute stereochemistry.



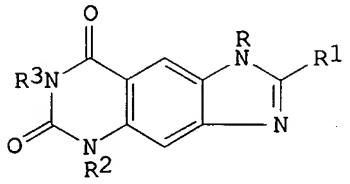
L4 ANSWER 45 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:48354 HCAPLUS
DOCUMENT NUMBER: 112:48354
TITLE: A study of the possible mechanisms underlying the convulsant actions of a linear expanded xanthine
AUTHOR(S): Collins, G. G. S.; Anson, J.
CORPORATE SOURCE: Univ. Dep. Pharmacol. Ther., R. Hallamshire Hosp., Sheffield, S10 2JF, UK
SOURCE: Pharmacology & Toxicology (Oxford, United Kingdom) (1989), 65(4), 306-12
CODEN: PHTOEH; ISSN: 0901-9928
DOCUMENT TYPE: Journal
LANGUAGE: English

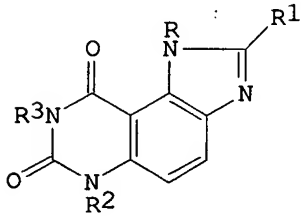
AB The actions of a mixture of the 4- and 9-chloro derivs. of the linear expanded xanthine 5,7-diethyl-2-chloroimidazo[4,5-g]quinazoline-6,8(5H,7H)-dione (chloro-DCQD) on the isolated olfactory cortex slice of the rat were investigated. Chloro-DCQD evoked a slowly developing depolarization which intensified over a drug administration period of ≥4 min. A pharmacol. investigation of the response showed that it was not mediated by blockade of K+ channels or activation of voltage-gated Na+ channels, by a stimulant action at receptors to GABA, excitatory amino acids or acetylcholine, or by antagonism of adenosine receptors. Chloro-DCQD (2.5 mM) potentiated responses evoked by N-methyl-D-aspartate (NMDA), L-aspartate and L-glutamate, probably by overcoming the Mg2+ block of the NMDA receptor complex. Chloro-DCQD (2.5 or 5 mM) also increased pyramidal cell excitability and abolished GABA-mediated postsynaptic inhibition but did not affect the excitability of, or neurotransmitter release from, the terminals of the lateral olfactory tract. Chloro-DCQD competitively antagonized the inhibitory actions of adenosine on the olfactory cortex. These effects are consistent with the reported convulsant actions of chloro-DCQD.

IT 107710-68-9
RL: BIOL (Biological study)
(convulsion from, mechanism of, brain neurophysiol. response in)
RN 107710-68-9 HCAPLUS
CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 2,9-dichloro-5,7-diethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 46 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:534091 HCAPLUS
DOCUMENT NUMBER: 111:134091
TITLE: Linear and proximal benzo-separated alkylated xanthines as adenosine-receptor antagonists
AUTHOR(S): Schneller, Stewart W.; Ibay, Augusto C.; Christ, William J.; Bruns, Robert F.
CORPORATE SOURCE: Dep. Chem., Univ. South Florida, Tampa, FL, 33620-5250, USA
SOURCE: Journal of Medicinal Chemistry (1989), 32(10), 2247-54
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:134091
GI

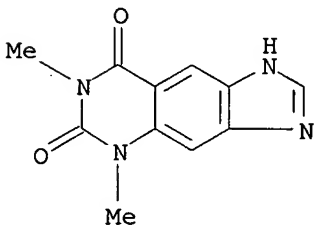

I


II

AB The linear and proximal benzo-separated derivs. I and II (R = H, Me; R1 = Ph, H; R2, R3 = alkyl) of 8-phenyltheophylline, 1,3-diethyl-8-phenyl-, 1,3-dipropyl-, 1,3-dibutyl-, or 3-isobutyl-1-methylxanthine, theophylline, caffeine, and isocaffeine have been synthesized from chloronitro-2,4(1H,3H)-quinazolinediones and evaluated for affinity at the A1 and A2 adenosine receptors. Although structure-activity relationships in the benzo-separated series differed from the relationships in the simple xanthines, the most potent of the benzo-separated xanthines were about equal in affinity to the most potent of the corresponding xanthines. It appears that the primary requirement for adenosine-receptor affinity in nonnucleosides is a flat, neutral, fused-ring heterocycle and that once this requirement is met there are numerous potential binding modes.

IT 76822-71-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(adenosine-receptor antagonist activity of)

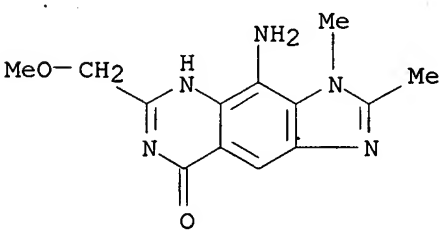
RN 76822-71-4 HCAPLUS
CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 5,7-dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 47 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:477957 HCAPLUS
DOCUMENT NUMBER: 111:77957
TITLE: Studies of extended quinone methides. Synthesis and physical studies of purine-like monofunctional and bifunctional imidazo[4,5-g]quinazoline reductive alkylating agents
AUTHOR(S): Lemus, Robert H.; Lee, Chang Hee; Skibo, Edward B.
CORPORATE SOURCE: Dep. Chem., Arizona State Univ., Tempe, AZ, 85287-1604, USA
SOURCE: Journal of Organic Chemistry (1989), 54(15), 3611-18
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:77957

AB Described herein are the synthesis, quinone methide reactivity, and electrochem. of purine-like imidazo[4,5-g]quinazoline reductive alkylating agents possessing a leaving group at the 6α-position. Also described is the synthesis of a dual alkylating analog possessing a leaving group at both the 2α- and 6α-positions. The reductive alkylating agent design involves leaving group placement on the 4,9-dione (quinone) derivative of the title ring system so as to permit formation of an alkylating quinone methide species upon reduction to the hydroquinone and elimination of the leaving group. The purine-like structure of these reductive alkylating agents may permit selective inactivation of purine-utilizing enzymes in low reduction potential tumor cells. Comparisons of our finding with those obtained for an analogous reductive alkylating system revealed the following: (i) lowering the quinone reduction potential greatly enhances the rate of leaving group elimination (e.g., a 2300-fold increase in the rate of chloride elimination accompanies a 200-mV potential decrease), and (ii) lower potentials favor electrophile trapping (ketonization) over nucleophile trapping of the quinone methide intermediate. The results of our studies indicate electrochem. studies are valuable in predicting the reactivity pattern of a reductive alkylating agent.

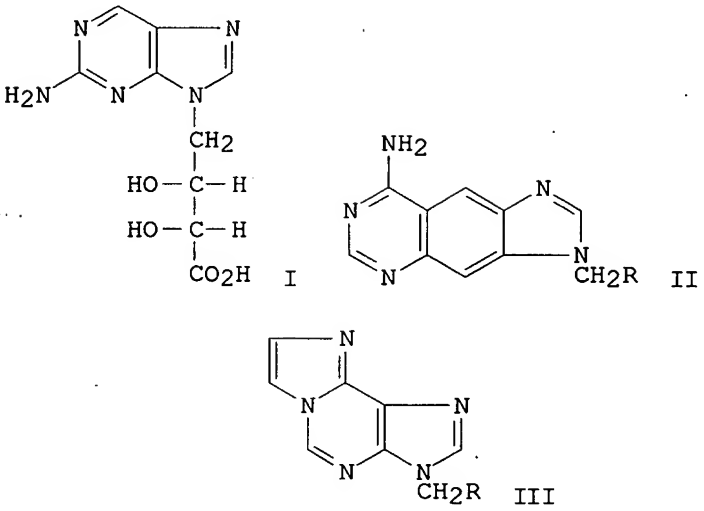
IT 121732-22-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and bromination of)
RN 121732-22-7 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 4-amino-3,5-dihydro-6-(methoxymethyl)-2,3-dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 48 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:193292 HCAPLUS
DOCUMENT NUMBER: 110:193292
TITLE: Studies on S-adenosyl-L-homocysteine hydrolase. XVII. Fluorescent analogs of acyclic inhibitors of S-adenosyl-L-homocysteine hydrolase

10/ 715,547

AUTHOR(S): Dvorakova, Hana; Holy, Antonin; Masojidkova, Milena
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1988), 53(8), 1779-94
CODEN: CCCCAK; ISSN: 0366-547X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:193292
GI



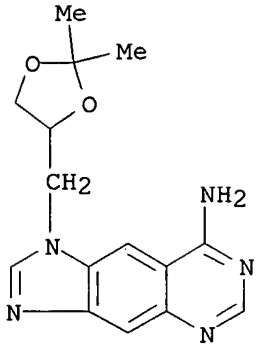
I II III

AB 9-(RS)-(2,3-Dihydroxypropyl)-2-aminopurine, erythro-(2R,3R)-4-(2-aminopurin-9-yl)- (I) and erythro-(2R,3R)-4-(2-aminopurin-7-yl)-2,3-dihydroxybutanoic acid, lin-benzoadenine derivs. II [R = CH(OH)CH2OH, (R,R)-CH(OH)CH(OH)CO2H], and 1,N6-ethenoadenine derivs. III [R = CH(OH)CH2OH, (R,R)-CH(OH)CH(OH)CO2H, CH(OH)CO2H, CH(OH)CO2CH2CHMe2, (S)-CH(CH2OH)OCH2P(O)(OH)2, CH2OCH2P(O)(OH)2] were prepared Thus, treatment of 2-aminopurine with NaH in DMF and addition of 2,3-O-cyclohexylidene-D-erythronolactone afforded 9.6% I and 3.2% of its 7-isomer. Fluorescence spectra of the synthesized compds. exhibit parameters corresponding to the substituted fluorophore; however, no pronounced inhibitory effect on S-adenosyl-L-homocysteine hydrolase from L-1210 mice leukemia cells was found.

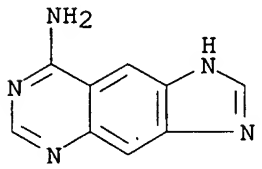
IT 120139-17-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and benzoylation of)

RN 120139-17-5 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazolin-8-amine, 1-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 49 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:172961 HCAPLUS
DOCUMENT NUMBER: 110:172961
TITLE: Defined dimensional alterations in enzyme substrates. Birch reduction of lin-benzopurines. A contribution to information concerning the binding sites of adenosine deaminase and xanthine oxidase
AUTHOR(S): Leonard, Nelson J.; Petric, Andrej; Rykowski, Andrzej
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801-3731, USA
SOURCE: Journal of Organic Chemistry (1988), 53(16), 3873-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:172961
AB Under carefully controlled Birch reduction conditions, 4,9-dihydro-lin-benzohypoxanthine (I) was prepared from lin-benzohypoxanthine, 4,9-dihydro-lin-benzoxanthine (II) from lin-benzoxanthine, 4,9-dihydro-lin-benzoguanine from lin-benzoguanine, and 4,9-dihydro-lin-benzoadenine (III) from lin-benzoadenine. III behaves neither as a substrate nor as an inhibitor with adenosine deaminase, whereas I is oxidized to II in the presence of xanthine oxidase.
IT 53449-12-0, 1H-Imidazo[4,5-g]quinazolin-8-amine
RL: RCT (Reactant); RACT (Reactant or reagent)
(Birch reduction of)
RN 53449-12-0 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine (CA INDEX NAME)



L4 ANSWER 50 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:200772 HCAPLUS
DOCUMENT NUMBER: 108:200772
TITLE: Allosteric nucleotide specificity of phosphorylase kinase: correlation of binding, conformational transitions, and activation. Utilization of lin-benzo-ADP to measure the binding of other

nucleoside diphosphates, including the phosphorothioates of ADP

AUTHOR(S): Cheng, Alexander; Fitzgerald, Thomas J.; Bhatnagar, Deepak; Roskoski, Robert, Jr.; Carlson, Gerald M.

CORPORATE SOURCE: Med. Cent., Univ. Mississippi, Jackson, MS, 39216, USA

SOURCE: Journal of Biological Chemistry (1988), 263(12), 5534-42
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

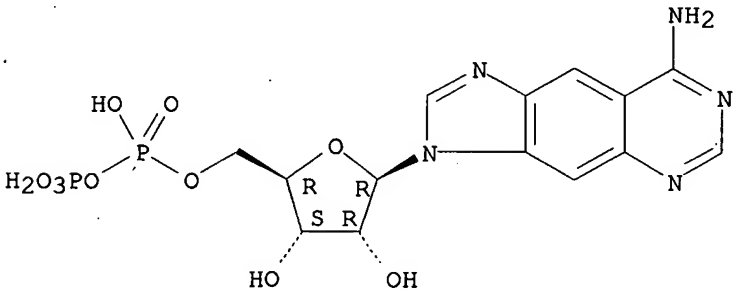
AB ADP is an allosteric activator of nonphosphorylated phosphorylase kinase from rabbit skeletal muscle (Cheng, A., et al., 1985). The specificity of the allosteric site for nucleoside diphosphates was further investigated. Only purine nucleoside diphosphates cause allosteric activation, and an NH2 group at position 2 or 6 of the purine ring is required. Comparisons are made of the abilities of 5'-diphosphate analogs of ADP, including phosphorothioates, to activate, to bind, and to induce the conformational changes in the enzyme β subunits associated with activation. Binding is measured by competition titrns. utilizing fluorescence polarization of lin-benzo-ADP, itself an allosteric activator, and conformational changes are measured by partial proteolysis and chemical crosslinking. When measured at an identical percentage of saturation at the allosteric site, the abilities of ADP analogs to induce conformational changes in the β subunits parallel their abilities to activate the holoenzyme. An unmodified β-phosphate of ADP, although not necessary for binding at the allosteric site, is needed to fully drive the activating conformational transition. The activating nucleoside diphosphate appears to be the free species, as opposed to its Mg2+ complex.

IT 61925-59-5, lin-Benzo-ADP
RL: BIOL (Biological study)
(phosphorylase kinase allosteric activation by, structure in relation to)

RN 61925-59-5 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 51 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:127574 HCAPLUS

DOCUMENT NUMBER: 108:127574

TITLE: Synthetic peptide analogs differentially alter the binding affinities of cyclic nucleotide-dependent protein kinases for nucleotide substrates

AUTHOR(S): Bhatnagar, Deepak; Glass, David B.; Roskoski, Robert, Jr.; Lessor, Ralph A.; Leonard, Nelson J.

CORPORATE SOURCE: South. Reg. Res. Cent., U.S. Dep. Agric., New Orleans, LA, 70179, USA

SOURCE: Biochemistry (1988), 27(6), 1988-94
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

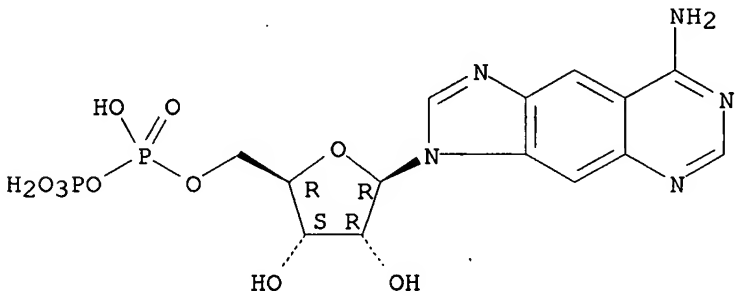
AB Analogs of a synthetic heptapeptide substrate corresponding to the sequence around a phosphorylation site in histone H2B were used to assess interactions between the peptide substrate and the ATP binding sites of cGMP-dependent protein kinase and the catalytic subunit of cAMP-dependent protein kinase. The affinity of each protein kinase for lin-benzo-ADP was determined in the absence and presence of substrate peptide by fluorescence anisotropy titrns. The dissociation constant (Kd) values of cGMP-dependent protein kinase for lin-benzo-ADP in the absence and presence of cGMP were 7.6 and 9.7 μM, resp. Histone H2B(29-35) (Arg-Lys-Arg-Ser-Arg-Lys-Glu) had no effect on nucleotide affinity in either the absence or presence of cGMP. However, when lysine-34, which is located 2 residues after the phosphorylatable serine-32, is replaced with an alanyl residue, the resulting [Ala34]histone H2B(29-35) and its analog peptides interacted with cGMP-dependent protein kinase and/or the nucleotide in a fashion that decreased nucleotide binding affinity .apprx.3-fold. This amino acid replacement was previously shown to increase the Vmax and decrease the pH optimum for the phosphotransferase reaction. The replacement of pos. charged residues at positions 30 and 31 of the peptide also decreased the nucleotide affinity. Other analogs of histone H2B(29-35) failed to affect binding of lin-benzo-ADP to the active site of the cGMP-dependent enzyme. The effect of peptides to decrease nucleotide binding affinity was greater on ADP than on the fluorescent ligand. None of the histone peptide analogs significantly altered adenine nucleotide binding to the catalytic subunit of cAMP-dependent protein kinase. Thus, histone H2B(29-35) peptides apparently interact with the peptide or nucleotide binding sites differently in the 2 protein kinases, possibly because the dimeric cGMP-dependent protein kinase contains a regulatory domain.

IT 61925-59-5
RL: BIOL (Biological study)
(protein kinase binding of, phosphorylation site peptide analogs effect on)

RN 61925-59-5 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 52 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:632021 HCAPLUS
DOCUMENT NUMBER: 107:232021

TITLE: Active-site-directed reductive alkylation of xanthine oxidase by imidazo[4,5-g]quinazoline-4,9-diones functionalized with a leaving group

AUTHOR(S): Lee, Chang Hee; Skibo, Edward B.

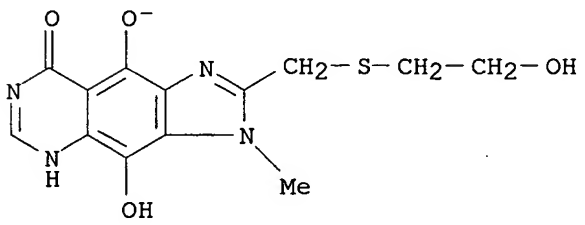
CORPORATE SOURCE: Dep. Chem., Arizona State Univ., Tempe, AZ, 85287, USA
SOURCE: Biochemistry (1987), 26(23), 7355-62
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new class of purine antimetabolites, directed toward xanthine oxidase, was designed by employing some of the features found in the bioreductive alkylator, mitomycin C. The design involved functionalizing the purine-like imidazo[4,5-g]quinazoline ring system as a quinone (4,9-dione) bearing a 2α leaving group. Due to the presence of the electron-deficient quinone ring, the leaving group could not participate in alkylation reactions. Reduction to the hydroquinone (4,9-dihydroxy) derivative, however, permitted elimination of the leaving group to afford an alkylating quinone methide. In spite of the electronic differences, both quinone and hydroquinone derivs. of the imidazo[4,5-g]quinazoline system were able to enter the purine-utilizing active site of the enzyme. Thus, the hypoxanthine-like quinone derivative [2-(bromomethyl)-3-methylimidazo[4,5-g]quinazoline-4,8,9(3H,7H)-trione] and its hydroquinone derivative can act as reducing substrates for the enzyme, resulting in conversion to the xanthine-like 6-oxo derivs. Hydrolysis studies described here indicated that the hypoxanthine-like hydroquinone derivative eliminates HBr to afford an extended quinone methide species. The observed alkylation of the enzyme by this derivative may thus pertain to quinone methide generation and nucleophile trapping during enzymic oxidation at the 6-position. Enzymic studies indicated that the hypoxanthine-like quinone is an oxidizing suicide substrate for the enzyme. Thus, the reduced enzyme transfers electrons to this quinone, and the resulting hydroquinone inactivates the enzyme. As with mitomycin C, reduction and quinone methide formation are necessary for alkylation by the title quinone. This system is therefore an example of a purine active-site-directed reductive alkylator. It was concluded that reductive alkylators of other purine-utilizing enzymes may be designed by functionalizing the imidazo[4,5-g]quinazoline system as described above. This assessment was based on the substrate tolerance of many purine-utilizing enzymes for this dimensionally altered form of the purine ring. The utility of these reductive alkylators may lie in their selective activation in low-potential tumor cells, perhaps with reduced xanthine oxidase acting as the activating enzyme.

IT 111435-80-4
RL: FORM (Formation, nonpreparative)
(formation of, in (bromomethyl)dihydroxymethylimidazoquinazolinone hydrolysis)

RN 111435-80-4 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 3,5-dihydro-4,9-dihydroxy-2-[[(2-hydroxyethyl)thio]methyl]-3-methyl-, ion(1-) (9CI) (CA INDEX NAME)



L4 ANSWER 53 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:477749 HCAPLUS
DOCUMENT NUMBER: 107:77749

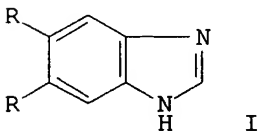
TITLE: Convenient synthesis of linear benzopurines through a

common intermediate

AUTHOR(S): Leonard, Nelson J.; Kazmierczak, Franciszek; Rykowski, Andrzej Z.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA

SOURCE: Journal of Organic Chemistry (1987), 52(13), 2933-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:77749

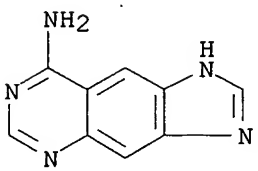
GI



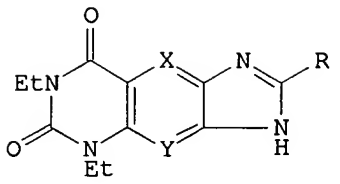
I

AB By the use of sym. substitution on benzimidazole, a common substituted isatoic anhydride precursor, for the convenient synthesis of lin-benzohypoxanthine, lin-benzoxanthine, lin-benzoguanine, and lin-benzoadenine, was prepared Thus, benzimidazole I (R = Me) was oxidized by KMnO4 to I (R = CO2H), which was converted with Ac2O to the anhydride. Treatment of the latter with Me3SiN3 gave the pivotal intermediate, a mixture of 1- and 3-acetylimidazo[4,5-g]benzoxazine-6,8(5H)-dione. Direct conversion of the mixture to the lin-benzopurines listed above was effected, resp., with formamidine acetate, urea, NCNH2, and tert-BuOK, and the sequence: anhydrous NH3, POCl3, and concentrated NH4OH.

IT 53449-12-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 53449-12-0 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine (CA INDEX NAME)



L4 ANSWER 54 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:156415 HCAPLUS
DOCUMENT NUMBER: 106:156415
TITLE: Linear expanded xanthines
AUTHOR(S): Rodgers, Gary R.; Neish, William J. P.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Sheffield, Sheffield, S10 2TN, UK
SOURCE: Monatshefte fuer Chemie (1986), 117(6-7), 879-82
CODEN: MOCMB7; ISSN: 0026-9247
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:156415
GI



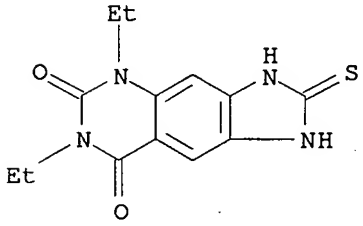
I

AB Expansion of the xanthine ring system has been accomplished by linear formation of a benzo, pyrido or pyrazino ring between the pyrimidine and imidazole portions I(X = CH; Y = CH, N; X = Y = N; R = OH, SH, Cl).

IT 107710-67-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of)

RN 107710-67-8 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 5,7-diethyl-2,3-dihydro-2-thioxo- (9CI) (CA INDEX NAME)



L4 ANSWER 55 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:15053 HCAPLUS

DOCUMENT NUMBER: 106:15053

TITLE: Synthesis, electrochemistry, and xanthine oxidase substrate reactivity of imidazo[4,5-g]quinazoline-4,9-diones. Studies directed toward the design of purine-like reductive alkylators

AUTHOR(S): Lee, Chang Hee; Gilchrist, James H.; Skibo, Edward B.

CORPORATE SOURCE: Dep. Chem., Arizona State Univ., Tempe, AZ, 85287, USA

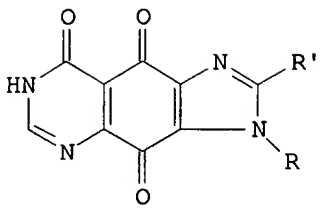
SOURCE: Journal of Organic Chemistry (1986), 51(25), 4784-92
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

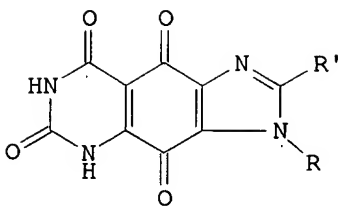
LANGUAGE: English

OTHER SOURCE(S): CASREACT 106:15053

GI



I



II

d R=Me R'=CH_2OMe III e R=Me R'=CH_2Br IV

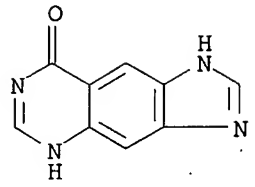
b R=Me R'=CH_2OMe V b R=R'=Me VI

AB The synthesis of imidazo[4,5-g]quinazoline-4,9-diones related to hypoxanthine and xanthine (I and II, resp.) was carried out in conjunction with the design of quinonelike purine mimics. These derivs. may exhibit purinelike binding to enzymes as well as quinone-mediated reactions such as reductive alkylation. Potential reductive alkylators were represented by compds. possessing a leaving group in the 2α-position: 2-(methoxymethyl)-3-methylimidazo[4,5-g]quinazoline-4,8,9(3H,7H)-trione (III), the 2-(bromomethyl) derivative of III (IV) and 2-(methoxymethyl)-3-methylimidazo[4,5-g]quinazoline-4,6,8,9(3H,5H,7H)-tetrone (V). The reduction of these systems, perhaps in low-potential tumor cells, should activate the leaving group and thereby facilitate the alkylation of purine-utilizing enzymes. Elaboration of the 4,9-dione (benzoquinone) moiety of I was carried out by either oxidation of 4-aminoimidazo[4,5-g]quinazoline derivs. with Fremy's radical or oxidation of 4,9-unsubstituted derivs. with NO2. The xanthine derivs. were prepared from I by xanthine oxidase-mediated oxidation A study of the enzymic oxidation of I to II (at pH 7.40) indicated that the associated catalytic parameters are comparable to those of the natural substrates, even though the hypoxanthine derivs. I exist largely in the anionic form and the natural substrates do not. Thus, the title quinones are purine mimics, at least in the case of xanthine oxidase oxidation Comparative electrochem. studies of 2,3-dimethylimidazo[4,5-g]quinazoline-4,8,9(3H,7H)-trione (VI) and 1,2-dimethylbenzimidazole-4,7-dione provided insights into the influence of the fused pyrimidine ring on the quinone redox potential. The neutral fused pyrimidine ring had no effect on the potential whereas the anionic form (pKa of VI = 6.15) lowered the potential. The expected low potentials for the title quinones at or above neutrality are desirable in terms of reductive alkylation; reduction will only occur in a low-potential environment. The electrochem. studies also revealed that a high-potential diprotonated quinone species (VI·H22+) is present in strong acid solns. In HBr solns., VI·H22+ readily oxidized Br- to Br2, presumably by 2-electron transfer from a bromo adduct. Thus, the design of reductive alkylators directed toward the active sites of purine-utilizing enzymes is feasible.

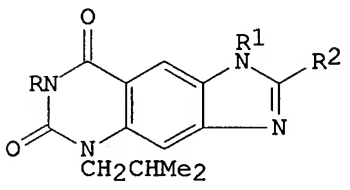
IT 53449-18-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidation and nitration of)

RN 53449-18-6 HCAPLUS

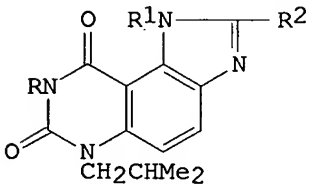
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro- (9CI) (CA INDEX NAME)



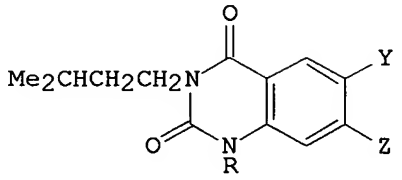
L4 ANSWER 56 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:424243 HCAPLUS
DOCUMENT NUMBER: 105:24243
TITLE: Inhibition of cyclic nucleotide phosphodiesterases from pig coronary artery by benzo-separated analogs of 3-isobutyl-1-methylxanthine
AUTHOR(S): Schneller, Stewart W.; Ibay, Augusto C.; Martinson, Elizabeth A.; Wells, Jack N.
CORPORATE SOURCE: Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA
SOURCE: Journal of Medicinal Chemistry (1986), 29(6), 972-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:24243
GI



I



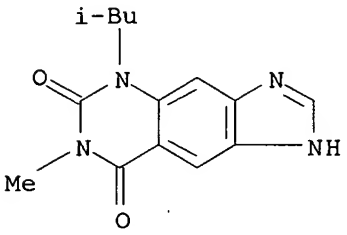
II



III

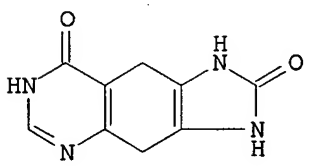
AB Imidazoquinazolines I and II (R = Me, R1 = H, R2 = H, Me, Me3C, CH2OMe; R = Me, R1 = PhCH2, R2 = H; R = Me2CHCH2CH2, R1 = R2 = H), benzo-separated analogs of the corresponding xanthine derivs., were prepared as inhibitors of the peak I and peak II of cyclic nucleotide phosphodiesterase from pig coronary artery. Thus, treating Me2CCH2CH2NCO with 4,2-Cl(H2N)C6H3CO2Me gave quinazoline III (R = Y = H, Z = Cl), which was successively nitrated to III (R = H, Y = NO2, Z = Cl), isobutylated to III (R = Me2CHCH2, Y = NO2, Z = Cl), and aminated to III (R = Me2CHCH2, Y = NO2, Z = NH2). Hydrogenation of the latter in HCO2H gave I (R = Me2CHCH2CH2, R1 = R2 = H). Analogously obtained was II (R, R1, R2 as above).
IT 101031-51-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzylation of, by benzyl chloride)
RN 101031-51-0 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 7-methyl-5-(2-methylpropyl)- (9CI) (CA INDEX NAME)

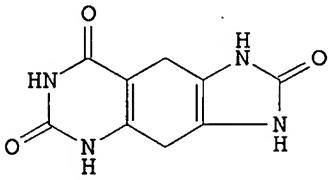


L4 ANSWER 57 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1986:109572 HCAPLUS
DOCUMENT NUMBER: 104:109572
TITLE: Defined dimensional alterations in enzyme substrates. General synthetic methodology for the bent dihydro-lin-benzopurines
AUTHOR(S): Stevenson, Thomas M.; Kazmierczak, Franciszek; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Journal of Organic Chemistry (1986), 51(5), 616-21
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 104:109572
GI



I

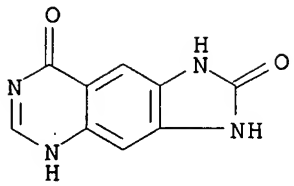


II

AB The use of cycloaddn. reactions for the synthesis of partially reduced heterocyclic systems has been shown to be an attractive approach to dihydrobenzimidazoles, dihydroquinazolines, and dihydro-lin-benzopurines. The first representatives of the bent dihydro-lin-benzopurines to be synthesized were 4,9-dihydroimidazo[4,5-g]quinazoline-2,8(1H,7H)-dione (I) and 4,9-dihydro-lin-benzouric acid (II).

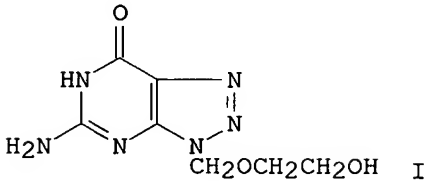
IT 99966-45-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 99966-45-7 HCAPLUS
CN 1H-Imidazo[4,5-g]quinazoline-2,8(3H,5H)-dione (9CI) (CA INDEX NAME)

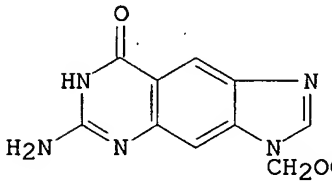


L4 ANSWER 58 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:437694 HCAPLUS
DOCUMENT NUMBER: 103:37694
TITLE: Modifications on the heterocyclic base of acyclovir: syntheses and antiviral properties
AUTHOR(S): Beauchamp, Lilia M.; Dolmatch, Bart L.; Schaeffer, Howard J.; Collins, Peter; Bauer, D. J.; Keller, Paul M.; Fyfe, James A.
CORPORATE SOURCE: Wellcome Res. Lab., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (1985), 28(8), 982-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:37694
GI



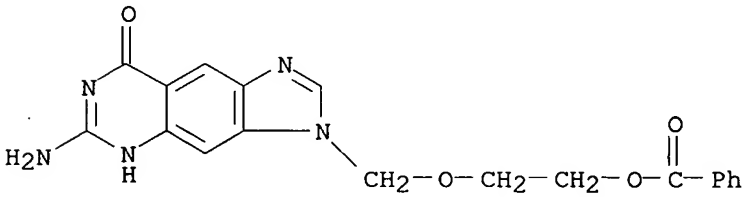
I



II

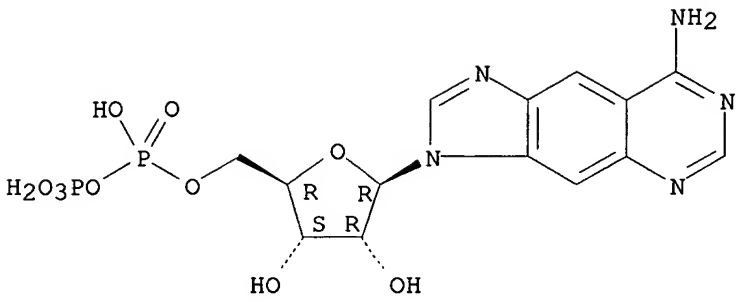
AB Several compds. were prepared in which variations of the ring portion of the acyclovir structure were made. These modifications included monocyclic (isocytosine, triazole, imidazole), bicyclic (8-azapurine, pyrrolo[2,3-d]pyrimidine, pyrazolo[3,4-d]pyrimidine) and tricyclic (linear benzoguanine) congeners. The derivs. were evaluated against herpes simplex virus type 1 (HSV-1) by the plaque-inhibition and plaque-reduction methods with only the 8-azapurine analog I showing some activity. In a test measuring the ability of these compds. to inhibit the HSV-1 thymidine kinase, I and the tricyclic derivative II exhibited competition with acyclovir for binding to the enzyme. The inability of the group to exert significant antiherpetic action is attributed to their lack of phosphorylation to the requisite triphosphate stage.
IT 96446-03-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
RN 96446-03-6 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 6-amino-3-[[2-(benzoyloxy)ethoxy]methyl]-3,5-dihydro- (9CI) (CA INDEX NAME)

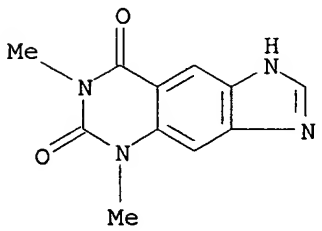


L4 ANSWER 59 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:108701 HCAPLUS
DOCUMENT NUMBER: 102:108701
TITLE: Interaction of guanosine cyclic 3',5'-phosphate dependent protein kinase with lin-benzoadenine nucleotides
AUTHOR(S): Bhatnagar, Deepak; Glass, David B.; Roskoski, Robert, Jr.; Lessor, Ralph A.; Leonard, Nelson J.
CORPORATE SOURCE: Med. Cent., Louisiana State Univ., New Orleans, LA, 70119, USA
SOURCE: Biochemistry (1985), 24(5), 1122-9
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using the activated cGMP-dependent protein kinase in the presence of the phosphorylatable peptide, Arg-Lys-Arg-Ser-Arg-Ala-Glu (I), it was found that lin-benzoadenosine 5'-diphosphate (lin-benzo-ADP) was a competitive inhibitor of the enzyme with respect to ATP, with a Ki (22 μM) similar to the dissociation constant (Kd) (20 μM) determined by fluorescence polarization titrns. The Kd for lin-benzo-ADP determined in the absence of the phosphorylatable peptide, however, was only 12 μM. ADP bound with lower affinity (Ki = 169 μM; Kd = 114 μM). With I as phosphoryl acceptor, the Km for lin-benzo-ATP was 29 μM and that for ATP was 32 μM. The Vmax with lin-benzo-ATP, however, was only 0.06% of that with ATP as substrate (0.00623 vs. 11.1 μmol/min/mg). The binding of lin-benzo-ADP to the kinase was dependent on a divalent cation. Fluorescence polarization revealed that Mg2+, Mn2+, Co2+s, Ni2+, Ca2+, Sr2+, and Ba2+ supported nucleotide binding to the enzyme; Ca2+, Sr2+, and Ba2+, however, did not support any measurable phosphotransferase activity. The rank order of metal ion effectiveness in mediating phosphotransferase activity was Mg2+ > Ni2+ > Co2+ > Mn2+. Although these results were similar to those previously observed with the cAMP-dependent protein kinase, major differences in the Vmax with lin-benzo-ATP as substrate and the effect of peptide substrates on nucleotide (both lin-benzo-ADP and ADP) binding were observed
IT 61925-59-5
RL: BIOL (Biological study)
(cGMP-dependent protein kinase inhibition by, kinetics of)
RN 61925-59-5 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 60 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:630483 HCAPLUS
DOCUMENT NUMBER: 101:230483
TITLE: The synthesis of lin-benzoreumycin, lin-1-methylbenzoxanthine, and lin-1,9-dimethylbenzoxanthine
AUTHOR(S): Schneller, Stewart W.; Ibay, Augusto C.; Christ, William J.
CORPORATE SOURCE: Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA
SOURCE: Journal of Heterocyclic Chemistry (1984), 21(3), 791-5
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Commencing with 7-chloro-3-methylquinazoline-2,4(1H,3H)-dione, a 5-step synthesis of 7-methylpyrimido[5,4-g]-1,2,4-benzotriazine-6,8(7H,9H)-dione (lin-benzoreumycin)(I) has been accomplished. A synthesis of 1,7-dimethylpyrimido[5,4-g]-1,2,4-benzotriazine-6,8(1H,7H)-dione (lin-benzotoxoflavin)(II) employing an intermediate from the preparation of I i.e., 7-chloro-3-methyl-6-nitroquinazoline-2,4(1H,3H)-dione (III) was attempted but could not be accomplished beyond the 1,4-dihydro precursor of II. III did lead to successful prepns. of 7-methylimidazo[4,5-g]quinazoline-6,8(5H,7H)-dione (lin-benzo-1-methylxanthine) and 3,7-dimethylimidazo[4,5-g]quinazoline-6,8(5H,7H)-dione (lin-benzo-1,9-dimethylxanthine) by reaction with NH2 or MeNH2 followed by reductive cyclization in HCO2H.
IT 76822-71-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 76822-71-4 HCAPLUS
CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 5,7-dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 61 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

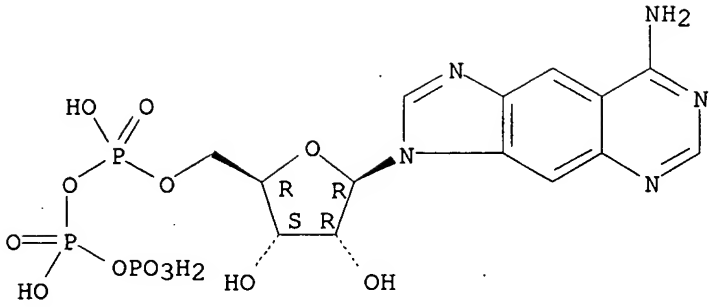
10/ 715,547

ACCESSION NUMBER: 1984:506455 HCAPLUS
DOCUMENT NUMBER: 101:106455
TITLE: Adenosine cyclic 3',5'-monophosphate dependent protein kinase: nucleotide binding to the chemically modified catalytic subunit
AUTHOR(S): Bhatnagar, Deepak; Hartl, F. Thomas; Roskoski, Robert, Jr.; Lessor, Ralph A.; Leonard, Nelson J.
CORPORATE SOURCE: Med. Cent., Louisiana State Univ., New Orleans, LA, 70119, USA
SOURCE: Biochemistry (1984), 23(19), 4350-7
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

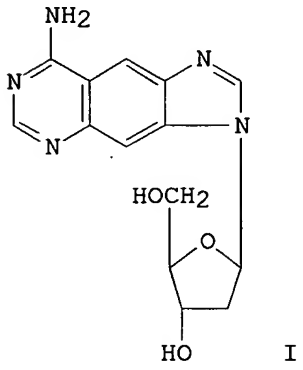
AB 5'-[p-(Fluorosulfonyl)benzoyl]adenosine (FSBA) inactivates the catalytic (C) subunit of cAMP-dependent protein kinase isolated from bovine cardiac muscle by covalent modification of lysine-71, whereas 7-chloro-4-nitro-2,1,3-benzoxadiazole (NBD-Cl) and 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB) react with cysteines-199 and -343 to inactivate the enzyme. All 3 of these reagents have been postulated to modify residues at or near the active site of the catalytic subunit. ATP (2 mM) in the presence of excess Mg2+ (10 mM) protected the enzyme against inactivation by these reagents. AMP did not afford any protection, but adenosine slightly decreased the rate of inactivation. The specific effects of covalent modification of lysine-71 and cysteines-199 and -343 on nucleotide binding were characterized by fluorescence polarization titrns. with lin-benzoadenine nucleotides as fluorescent ligands. lin-Benzoadenosine was a competitive inhibitor of the catalytic subunit with respect to ATP with a Ki (38 μM) similar to the Ki for adenosine (35 μM). This value agreed well with the dissociation constant (Kd) (32 μM) for adenosine determined by fluorescence polarization titrns. lin-Benzo-ADP was previously shown to be a competitive inhibitor with respect to ATP and lin-benzo-ATP was a substrate for the phosphotransferase activity of the protein kinase. Modification by FSBA, NBD-Cl, or DTNB resulted in >85% inhibition of phosphotransferase activity as well as complete inhibition of lin-benzo-ADP and lin-benzo-ATP binding in the presence of 10 mM Mg2+. lin-Benzoadenosine, on the other hand, bound to the enzyme with the same Kd and stoichiometry (1 mol/mol) as it did to the unmodified enzyme (Kd = 26-35 μM). Whereas all effectively displaced lin-benzoadenosine bound to the unmodified catalytic subunit, AMP, but not MgATP or MgADP, displaced the fluorescent probe from enzyme modified with NBD-Cl, DTNB, or FSBA. The Kd for AMP (804-856 μM), however, was 25% greater for the modified enzyme. These reagents, which are thought to modify residues that are at or near the active site of the catalytic subunit, inactivated the enzyme by inhibiting nucleotide binding. This effect involved the region on the C subunit complementary to the β- and γ-phosphates of the ATP mol. as compared to the region complementary to the α-phosphate of the nucleotide binding portion of the C subunit.

IT 61925-58-4
RL: BIOL (Biological study)
(protein kinase binding of, chemical modification effect on)
RN 61925-58-4 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 62 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:473045 HCAPLUS
DOCUMENT NUMBER: 101:73045
TITLE: Synthesis and biochemical evaluation of 2'-deoxy-lin-benzoadenosine phosphates
AUTHOR(S): Lessor, Ralph A.; Gibson, Katharine J.; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Biochemistry (1984), 23(17), 3868-73
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB 2'-Deoxy-lin-benzoadenosine (I) was prepared via reductive deoxygenation of 3-(β-D-ribofuranosyl)-8-(methylthio)imidazo[4,5-g]quinazoline. The 5'-mono-, 5'-di-, and 5'-triphosphates were prepared by chemical and/or enzymic methods. The 5'-diphosphate was found to be a substrate for phosphorylation by pyruvate kinase and was compared with various natural and extended substrates in kinetic assays. When I 5'-triphosphate was tested in a nick-translation experiment with Escherichia coli DNA polymerase I, a very low level of 32P incorporation from [α-32P]TTP into poly[d(AT)] was observed Nearest-neighbor anal. indicated that the analog was not significantly incorporated into internal positions in the polymer. In DNA-sequencing reactions, the analog caused chain termination at adenine residues, although termination was less uniform and less efficient than that with 2',3'-dideoxy-ATP. These expts. show that lin-benzoadenine can form a widened Watson-Crick base pair with thymine. They strongly

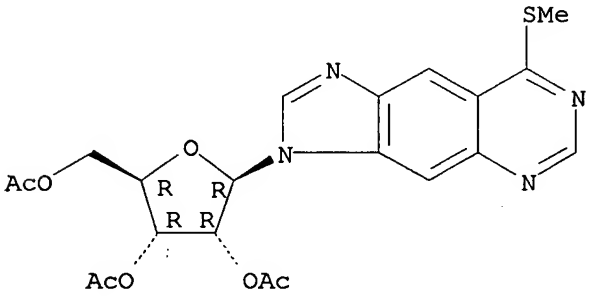
suggest, though they do not prove, that the enzyme is able to attach the analog to DNA.

IT 60189-86-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(partial deacetylation of)

RN 60189-86-8 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazoline, 8-(methylthio)-3-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 63 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:2711 HCAPLUS

DOCUMENT NUMBER: 100:2711

TITLE: Adenosine cyclic 3',5'-monophosphate dependent protein kinase: a new fluorescence displacement titration technique for characterizing the nucleotide binding site on the catalytic subunit

AUTHOR(S): Bhatnagar, Deepak; Roskoski, Robert, Jr.; Rosendahl, Mary S.; Leonard, Nelson J.

CORPORATE SOURCE: Med. Cent., Louisiana State Univ., New Orleans, LA, 70119, USA

SOURCE: Biochemistry (1983), 22(26), 6310-17
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The dissociation constant (Kd) of a series of nucleotides was determined for the bovine skeletal muscle type II catalytic subunit by displacing lin-benzo-ADP with increasing concns. of competing nucleotide. The Kd of each nucleotide was calculated from the decreases in the fluorescence polarization of lin-benzo-ADP that accompanied its displacement from the catalytic subunit. It was found that modifications of the adenine moiety reduced the nucleotide affinity for the enzyme. The effect was most pronounced with modifications at position 6 of the base. Replacement of the 3'-hydroxyl group of ribose with a H atom increased the affinity of the nucleotide; addition of phosphate to the 2'- or 3'-hydroxyl groups, on the other hand, decreased the nucleotide affinity. MgATP and MgADP exhibited Kd values of .apprx.10 μM. AMP, which contains a neg. charged α-phosphate, bound with much reduced affinity (643 μM). Adenosine, which lacks a charged α-phosphate, bound with a higher affinity (32 μM). To learn more about the nature of the α-phosphate binding site, a series of uncharged and pos. charged derivs. of the 5'-position on the ribose moiety was prepared The uncharged derivs. bound with much greater affinity than the neg. charged AMP. The Kd values for 5'-tosyladenosine and 5'-iodo-5'-deoxyadenosine were 30 and 32 μM, resp. Like the neg. charged AMP, pos. charged derivs. also bound less tenaciously than the neutral species. The pos. charged

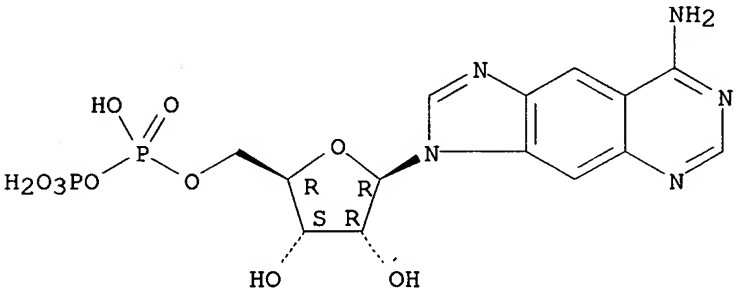
5'-amino-5'-deoxyadenosine exhibited a 15-fold higher Kd (506 μM) than the neutral congeners. It was hypothesized that the enzyme site complementary to the α-phosphate is hydrophobic in nature. Adding hydrophobic groups to the pos. charge at the 5'-position increased the binding affinity [Kd values for 5'-(ethylamino)-, 5'-(diethylamino)-, 5'-(triethylammonium)-, and 5'-(diallylamino)-5'-deoxyadenosine were 403, 284, 153, and 102 μM, resp.]. The binding of lin-benzo-ADP to the catalytic subunit of protein kinase was dependent on a divalent cation. Several metals were tested for their ability to promote binding and to support phosphotransferase activity. Fluorescence polarization studies revealed that Mg2+, Mn2+, Co2+, Cd2+, Ca2+, and Sr2+ supported nucleotide binding to the catalytic subunit, whereas Ba2+, Cr2+, Fe2+, Ni2+, Zn2+, Cu2+, Gd3+, and La3+ did not. Even though Ca2+ and Sr2+ promoted nucleotide binding, no measurable phosphotransferase activity was observed in their presence.

IT 61925-59-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cAMP-dependent protein kinase, kinetics of, structure in relation to)

RN 61925-59-5 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 64 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:175439 HCAPLUS

DOCUMENT NUMBER: 98:175439

TITLE: Adenosine cyclic 3',5'-monophosphate-dependent protein kinase: Interaction of the catalytic subunit and holoenzyme with lin-benzoadenine nucleotides

AUTHOR(S): Hartl, F. Thomas; Roskoski, Robert, Jr.; Rosendahl, Mary S.; Leonard, Nelson J.

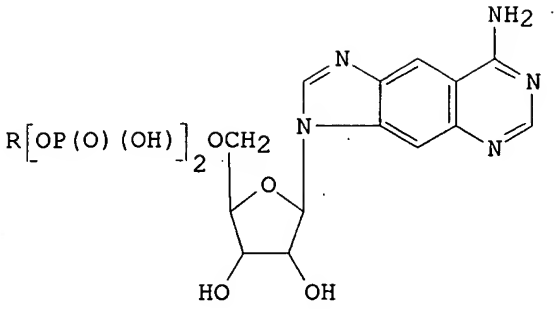
CORPORATE SOURCE: Med. Cent., Louisiana State Univ., New Orleans, LA, 70119, USA

SOURCE: Biochemistry (1983), 22(10), 2347-52
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I, R=H
II, R=P(O)(OH)2

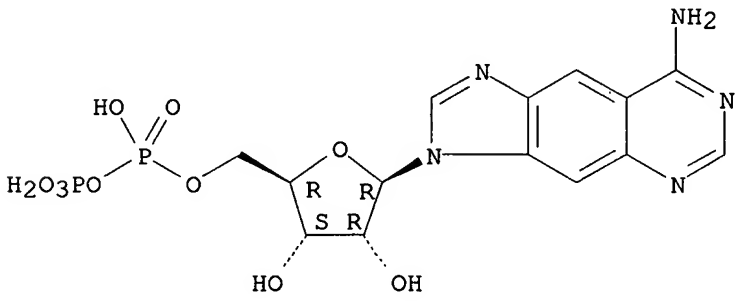
AB The interaction of lin-benzo-ADP (I) and lin-benzo-ATP (II) with the catalytic subunit and type II holoenzymes of cAMP-dependent protein kinase was investigated by steady-state kinetics and fluorescence spectroscopy. I was a competitive inhibitor of the catalytic subunit with respect to ATP with a Ki (8.0 μM) similar to the Ki for ADP (9.0 μM). This value agreed well with the Kd (9.0 μM) determined by fluorescence polarization titration Type II holoenzymes from bovine brain and skeletal muscle had Kd values for I of 3.4 and 3.5 μM, resp., and each bound .apprx.2 mol/mol of R2C2 tetramer. Furthermore, fluorescence polarization studies indicated that both the catalytic subunit and type II holoenzyme bound I rigidly, so that there was little or no rotation of the lin-benzoadenine portion of the mol. within the nucleotide-binding site. II was a substrate for the phosphotransferase activities of protein kinase with peptides, water, or type II regulatory subunit as phosphoryl acceptors. With Leu-Arg-Arg-Ala-Ser-Leu-Gly as phosphoryl acceptor, the Km for II was 11.3 μM, and that for ATP was 11.9 μM. The Vmax with lin-benzo-ATP was 20% of that with ATP as substrate. Thus, II is the best nucleotide substrate (besides ATP) for the catalytic subunit reported. 1,N6-Etheno-ATP (εATP), on the other hand, was a poor substrate for the catalytic subunit with a Km of 1.8 mM and a Vmax that was 4% of that for ATP, making it unsuitable as a fluorescent probe for cAMP-dependent protein kinase.

IT 61925-59-5
RL: BIOL (Biological study)
(protein kinase inhibition by, kinetics of)

RN 61925-59-5 HCAPLUS

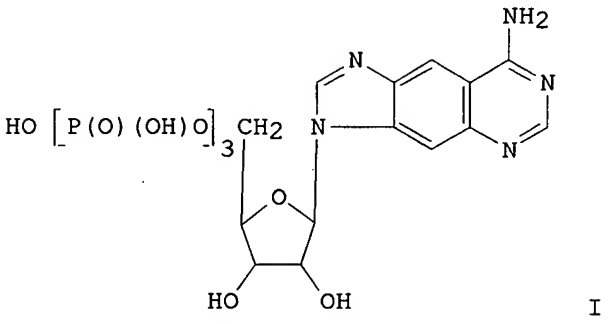
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 65 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:506190 HCAPLUS

DOCUMENT NUMBER: 97:106190
TITLE: Dimensional probing of the ATP binding site on firefly luciferase
AUTHOR(S): Rosendahl, Mary S.; Leonard, Nelson J.; Deluca, Marlene
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Photochemistry and Photobiology (1982), 35(6), 857-61
CODEN: PHCBAP; ISSN: 0031-8655
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

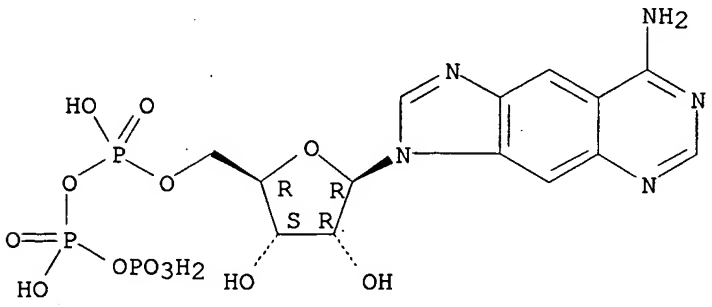
AB lin-Benzoadenosine 5'-triphosphate (I) has previously been shown to be an acceptable substrate for light production in the firefly luciferase-luciferin system. This nucleotide analog displayed strong enzyme binding and a reduced rate of enzyme catalysis compared with ATP. Variation in the color of the bioluminescence emission with I compared with ATP suggested that the lateral extension in the purine base induced a change in the conformation of the luciferase and in the environment of the excited light emitter.

IT 61925-58-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with firefly luciferase, kinetics and bioluminescence of)

RN 61925-58-4 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

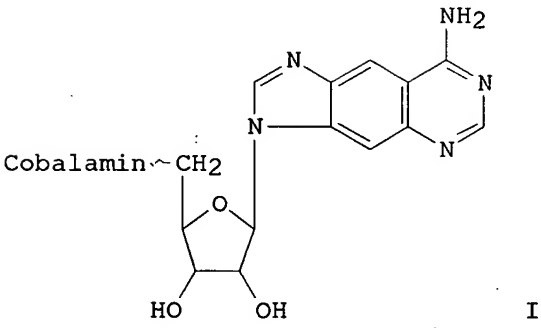
Absolute stereochemistry.



L4 ANSWER 66 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

10/ 715,547

ACCESSION NUMBER: 1982:468388 HCAPLUS
DOCUMENT NUMBER: 97:68388
TITLE: Synthesis and biological activity of a profluorescent analog of coenzyme B12
AUTHOR(S): Rosendahl, Mary S.; Omann, Geneva M.; Leonard, Nelson J.
CORPORATE SOURCE: Dep. Chem., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1982), 79(11), 3480-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



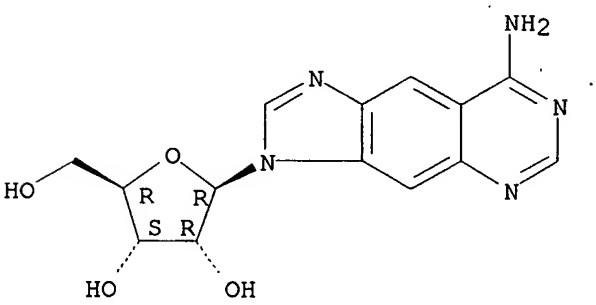
I

AB The synthesis and chemical properties of linear(lin)-benzoadenosylcobalamin (I), a coenzyme B12 analog that has a laterally extended nucleoside in the upper axial position, are described. I is an effective competitive inhibitor of ribonucleotide reductase from Lactobacillus leichmannii. I is nonfluorescent in solution, but on homolytic (light) or heterolytic (acid, CN-) cleavage of the C-Co bond it forms fluorescent products. In addition, fluorescence is detectable on binding of I to ribonucleotide reductase, and the observed fluorescence polarization of the lin-benzoadenosyl moiety indicates that it is bound loosely to the enzyme when the coenzyme is partially dissociated

IT 60189-62-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(chlorination of)

RN 60189-62-0 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

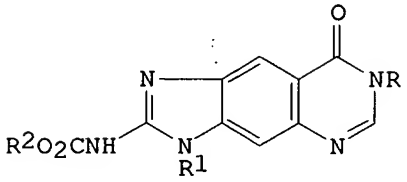
Absolute stereochemistry.



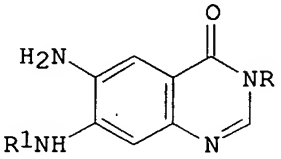
L4 ANSWER 67 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1982:438906 HCAPLUS
DOCUMENT NUMBER: 97:38906
TITLE: Possible anthelmintic agents: syntheses of various imidazoquinazolinone carbamates
AUTHOR(S): Kumar, Shiv; Kansal, V. K.; Bhaduri, A. P.
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1981), 20B(12), 1068-71
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 97:38906

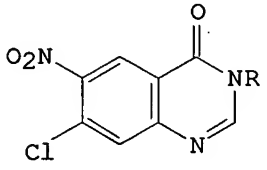
GI



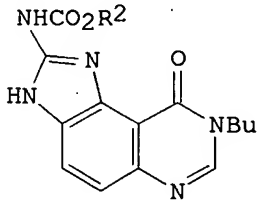
I



II



III



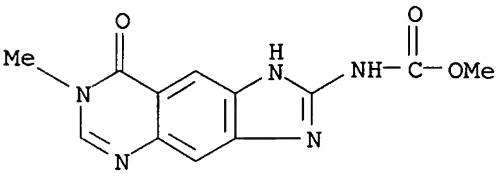
IV

AB Ten imidazoquinazolines I [R = H, Me, Bu, heptyl; R1 = H, PhCH2, Ph(CH2)3, HOCH2CH2; R2 = Me, Et] were prepared by cyclization of the diaminoquinazolines II with MeSC(:NH)NH2.H2SO4 and ClCO2R2. II were prepared in 4 steps from the chloroquinazolinone III (R = H). The imidazoquinazolines IV (R2 = Me, Et) were similarly prepared from the corresponding diaminoquinazoline. III (R = H, Bu) reacted with NH3 to give ring opened products. At 100 mg/kg I caused 100% clearance of Hymenolepis nana.

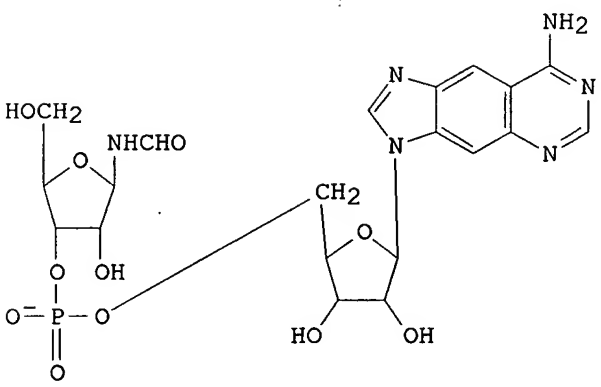
IT 81946-14-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anthelmintic activity of)

RN 81946-14-7 HCAPLUS

CN Carbamic acid, (7,8-dihydro-7-methyl-8-oxo-1H-imidazo[4,5-g]quinazolin-2-yl)-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 68 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:181564 HCAPLUS
DOCUMENT NUMBER: 96:181564
TITLE: Foreshortened nucleotide analogs as potential base-pairing complements for lin-benzoadenosine
AUTHOR(S): Czarnik, Anthony W.; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Journal of the American Chemical Society (1982), 104(9), 2624-31
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Syntheses of foreshortened nucleotide analogs of uridine have been carried out to test the possibility of base pairing with the linearly extended nucleoside lin-benzoadenosine. Phosphorylation of N-(β-D-ribofuranosyl)formamide (F) provided the 5-monophosphate, which could be dephosphorylated by the action of either alkaline phosphatase or, surprisingly, 5'-nucleotidase. Addnl. phosphorylations by the method of D. E. Hoard and D. G. Ott (1965) afforded the 5-di- and -triphosphates. The diphosphate, 5-FDP, did not undergo polymerization with polynucleotide phosphorylase. Syntheses of the self-complementary dinucleoside monophosphates FpA and Fp(lin-benzo-A) (I) are described. The foreshortened analog was protected as its 2-(methoxytetrahydropyranyl)-5-(tert-butyldiphenylsilyl) derivative, while 5'-AMP and lin-benzo-AMP were protected by new and easy method as the corresponding 2,3'-di-O-(tert-butyldimethylsilyl) nucleotides. Condensation of the fully protected F and 5'-monophosphate moieties provided the desired (3→5')-linked nucleotides, which, on treatment with phosphodiesterase I, were hydrolyzed back to F and the corresponding 5'-monophosphate.

IT 80963-99-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and coupling reaction of, with ribofuranosylformamide derivative)

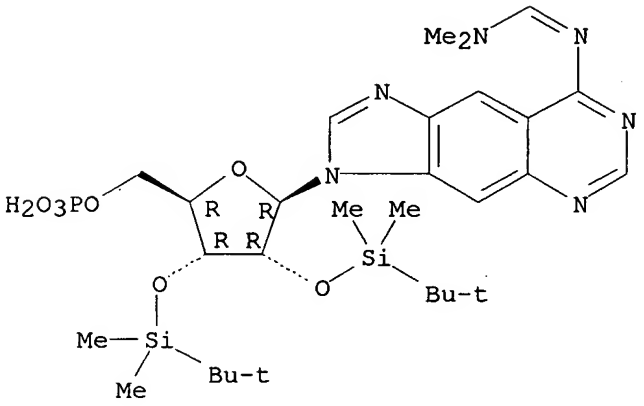
RN 80963-99-1 HCAPLUS
CN Methanimidamide, N'-[3-[2,3-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-5-O-phosphono-β-D-ribofuranosyl]-3H-imidazo[4,5-g]quinazolin-8-yl]-N,N-

dimethyl-, compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 80963-98-0
CMF C29 H49 N6 O7 P Si2

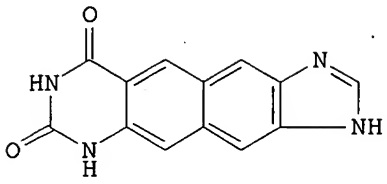
Absolute stereochemistry.
Double bond geometry unknown.



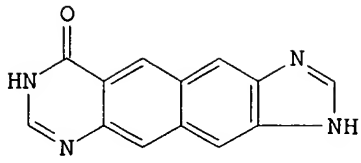
CM 2

CRN 110-86-1
CMF C5 H5 N

L4 ANSWER 69 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:176800 HCAPLUS
DOCUMENT NUMBER: 96:176800
TITLE: Defined dimensional alterations in enzyme substrates. Synthesis and enzymic evaluation of some lin-naphthopurines
AUTHOR(S): Moder, Kenneth P.; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Journal of the American Chemical Society (1982), 104(9), 2613-24
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



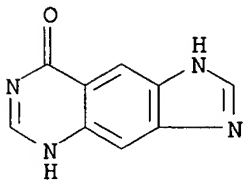
II

AB The development of methodol. for the regioselective syntheses of tetra-β-substituted naphthalenes via a combination of bicyclo[4.2.0]octa-1,3,5-triene and aryl trimethylsilyl chemical led to the synthesis of benzimidazo[5,6-g]-6H,8H-quinazoline-7,9-dione (lin-naphthoxanthine) (I) and benzimidazo[5,6-g]-8H-quinazolin-9-one (lin-naphthohypoxanthine) (II), 4.8-Å laterally extended dimensional derivs. of xanthine and hypoxanthine, resp. I and II exhibited intense fluorescence. I was not oxidized to lin-naphthouric acid by xanthine oxidase, but functioned as a noncompetitive inhibitor. However, II was readily converted to I by xanthine oxidase. In this reaction, II functioned as a competitive inhibitor of xanthine oxidase. The enzymic results for the naphtho analogs when compared with the benzo analogs demonstrated, in part, a useful application of defined dimensional probes for determining the limiting spatial restrictions of the binding region for xanthine oxidase.

IT 53449-18-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with xanthine oxidase, kinetics of)

RN 53449-18-6 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 70 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:192283 HCAPLUS

DOCUMENT NUMBER: 94:192283

TITLE: Synthesis of lin-benzofervenulin, lin-benzotheophylline, and lin-benzocaffeine

AUTHOR(S): Schneller, Stewart W.; Christ, William J.

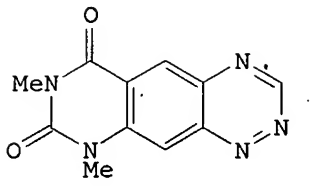
CORPORATE SOURCE: Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA

SOURCE: Journal of Organic Chemistry (1981), 46(8), 1699-702
CODEN: JOCEAH; ISSN: 0022-3263

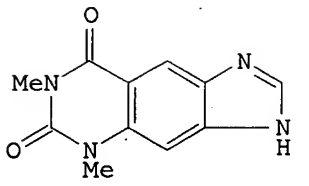
DOCUMENT TYPE: Journal

LANGUAGE: English

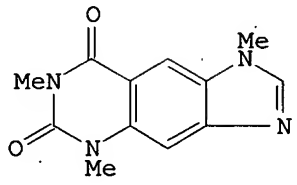
GI



I



II



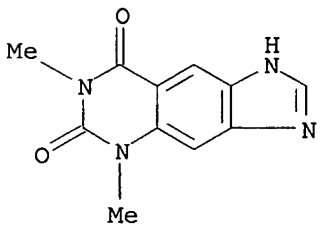
III

AB The synthesis of the pyrimidobenzotriazinedione (I) as the lin-benzo-separated analog of fervenulin is reported in five steps from 7-chloro-2,4(1H,3H)-quinazolinedione. The preparation of lin-benzotheophylline (II) is described as arising from 1,3-dimethyl-7-hydrazino-6-nitro-2,4(1H,3H)-quinazolinedione in a procedure originally designed to give I. Methylation of II gave two products, one of which is lin-benzocaffeine III.

IT 76822-71-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 76822-71-4 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline-6,8(5H,7H)-dione, 5,7-dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 71 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:60541 HCAPLUS

DOCUMENT NUMBER: 94:60541

TITLE: Activation of cyclic AMP-dependent protein kinases I and II by cyclic 3',5'-phosphates of 9-β-D-ribofuranosylpurine and 1-β-D-ribofuranosylbenzimidazole

AUTHOR(S): Yagura, Terry S.; Kazimierczuk, Zygmunt; Shugar, David; Miller, Jon P.

CORPORATE SOURCE: Life Sci. Div., SRI Int., Menlo Park, CA, 94025, USA

SOURCE: Biochemical and Biophysical Research Communications (1980), 97(2), 737-43
CODEN: BBRCA9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

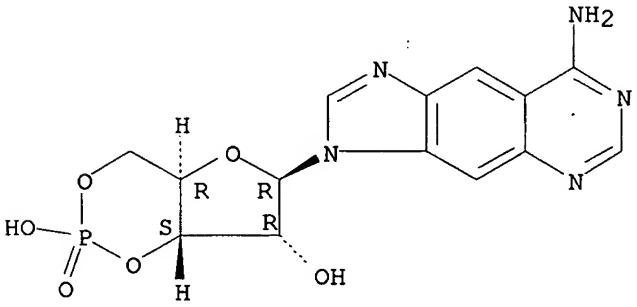
LANGUAGE: English

AB Analogs of cAMP lacking the 6-NH2 group (9-β-D-ribofuranosylpurine cyclic 3',5'-phosphate) (I), or the 1- and 3-N atoms as well as the 6-NH2

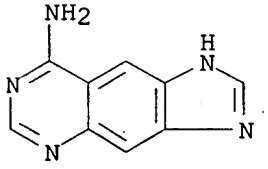
group (1-β-D-ribofuranosylbenzimidazole cyclic 3',5'-phosphate) (II), were effective activators of both type I (cAKI) and type II (cAKII) isoenzymes of cAMP-dependent protein kinase. An analog with a pyrimidine ring fused to the benzimidazole ring system of II (3-β-D-ribofuranosyl-8-aminoimidazo[4,5-g]quinazoline cyclic 3',5'-phosphate), was as potent as I or II as an activator of cAKII but only 1/10 as potent as I or II as an activator of cAKI. Thus, neither isoenzyme requires the 6-NH2 group; however, they may have different sensitivities to alterations in the electron distribution of the pyrimidine ring.

IT 61925-60-8
RL: BIOL (Biological study)
(protein kinase isoenzyme activation by)
RN 61925-60-8 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-(3,5-O-phosphinico-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 72 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:159661 HCAPLUS
DOCUMENT NUMBER: 92:159661
TITLE: Molecular and biological properties of lin-benzoadenine derivatives
AUTHOR(S): Vanderlijn, Pieter John
CORPORATE SOURCE: Univ. Illinois, Urbana, IL, USA
SOURCE: (1979) 120 pp. Avail.: Univ. Microfilms Int., Order No. 8004294
From: Diss. Abstr. Int. B 1980, 40(8), 3724
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT 53449-12-0D, derivs.
RL: BIOL (Biological study)
(enzyme response to)
RN 53449-12-0 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine (CA INDEX NAME)



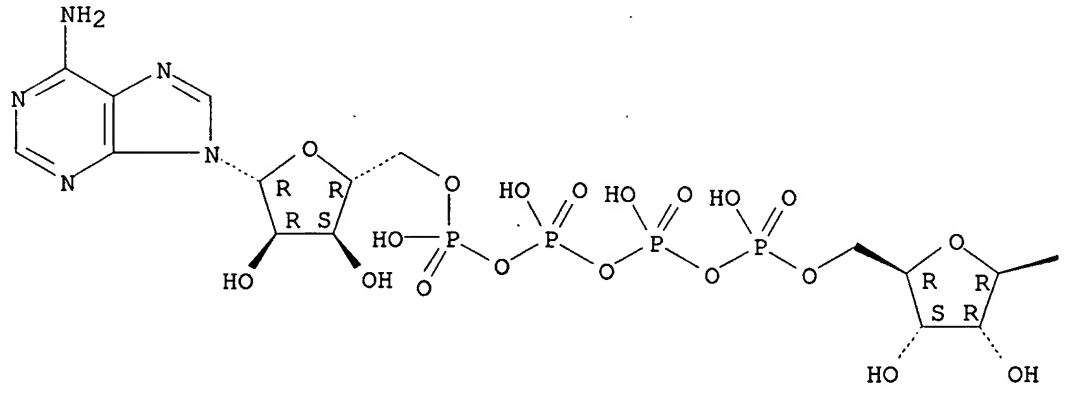
L4 ANSWER 73 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:2245 HCAPLUS
DOCUMENT NUMBER: 92:2245
TITLE: Inhibition of adenylate kinase by P1-(lin-benzo-5'-adenosyl)-P4-(5'-adenosyl) tetraphosphate and P1-(lin-benzo-5'-adenosyl)-P5-(5'-adenosyl) pentaphosphate
AUTHOR(S): VanDerLijn, Pieter; Barrio, Jorge R.; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Biochemistry (1979), 18(25), 5557-61
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

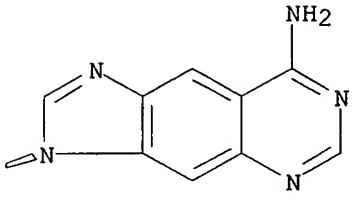
AB P1-(lin-Benzo-5'-adenosyl)-P5-5'-adenosyl pentaphosphate and P1-(lin-benzo-5'-adenosyl-P4-(5'-adenosyl) tetraphosphate were synthesized from lin-benzoadenosine 5'-monophosphoromorpholidate and adenosine 5'-tetraphosphate and ATP. These mixed dinucleoside polyphosphates were potent inhibitors of porcine muscle adenylate kinase, with association consts. of 2 + 105 M-1 for the pentaphosphate and 2 + 106 M-1 for the tetraphosphate, resp., as determined by kinetics and fluorescence expts. The increase in fluorescence intensities and fluorescence lifetimes of both inhibitors on binding to adenylate kinase results from a breaking of the intramol. stacking interaction observed when these ligands are free in solution and implicates their binding to the enzyme in an open or extended form. These results and the dimensional requirements of these inhibitors are discussed in relation to current knowledge of the active site of adenylate kinase and to the known inhibitors of adenylate kinase, P1,P5-bis(5'-adenosyl) pentaphosphate and P1,P4-bis(5'-adenosyl) tetraphosphate.

IT 72040-60-9
RL: BIOL (Biological study)
(adenylate kinase inhibition by)
RN 72040-60-9 HCAPLUS
CN Adenosine 5'-(pentahydrogen tetraphosphate), P'''→5'-ester with 3-β-D-ribofuranosyl-3H-imidazo[4,5-g]quinazolin-8-amine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



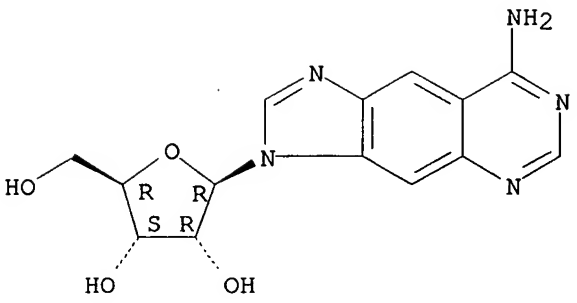


L4 ANSWER 74 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:353 HCAPLUS
DOCUMENT NUMBER: 92:353
TITLE: Coronary vasoactivity of adenosine in the conscious dog
AUTHOR(S): Olsson, Ray A.; Khouri, Edward M.; Bedynek, Julius L., Jr.; McLean, John
CORPORATE SOURCE: Dep. Cardiorespiratory Dis., Walter Reed Army Inst. Res., Washington, DC, USA
SOURCE: Circulation Research (1979), 45(4), 468-78
CODEN: CIRUAL; ISSN: 0009-7330
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Intracoronary adenosine [58-61-7] infusions into conscious dogs produced half-maximal coronary vasodilation at 0.57 μM, similar activity was shown by 1.01 μM adenosine in open-chest dogs. In both prepns., adenosine at concns. in the range found in cardiac muscle by direct anal. produced coronary vasodilation equal to that attained during a maximum reactive hyperemic response. The quant. structure-activity relationship technique was applied to data on the coronary vasoactivity of 68 adenosine analogs to identify the chemical features of this mol. that determine its vasoactivity. These are: (1) the size of the purine base; (2) the inductive effect of the C-2 substituent; (3) the electron-withdrawing effect of the C-6 substituent; (4) the glycosylic torsion angle; (5) the ability of the C-2' and C-3'-hydroxyls to participate in H bonding; (6) the absence of sterically hindering groups in the vicinity of C-2' and, more importantly, C-3'; and (7) the inductive effect of the C-5' substituent. The hydrophobicity of these analogs did not correlate with vasoactivity. The hydrophilicity of the ribose moiety apparently overshadows any hydrophobic influence of the very weakly aromatic purine base.

IT 60189-62-0
RL: BIOL (Biological study)
(heart circulation response to, adenosine in relation to)
RN 60189-62-0 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

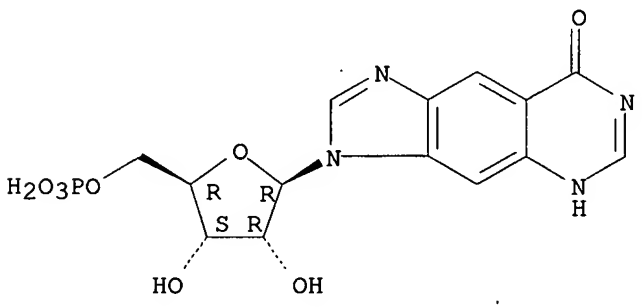


L4 ANSWER 75 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:605799 HCAPLUS
DOCUMENT NUMBER: 91:205799
TITLE: Synthesis of fluorescent nucleotide analogs: 5'-mono-, di-, and triphosphates of linear-benzoguanosine, linear-benzoinosine, and linear-benzoxanthosine
AUTHOR(S): Leonard, Nelson J.; Keyser, Gene E.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1979), 76(9), 4262-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The fluorescent nucleotide analogs (the 5'-mono-, di-, and triphosphates of lin-benzoguanosine, lin-benzoxanthosine, and lin-benzoinosine) were prepared for use as dimensional probes of enzyme binding sites. They have quantum yields in aqueous solution of 0.39, 0.55, and 0.04 and fluorescent lifetimes of 6, 9, and .apprx.1.5 ns, resp. lin-Benzoinosine 5'-monophosphate is a substrate for xanthine oxidase (EC 1.2.3.2), providing lin-benzoxanthosine 5'-monophosphate, and lin-benzoinosine 5'-diphosphate is a substrate for polynucleotide phosphorylase (EC 2.7.7.8), giving poly(lin-benzoinosinic acid). The benzologs of the purine diphosphates are substrates for pyruvate kinase (EC 2.7.1.40), which is used to prepare the triphosphates.

IT 72006-37-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as enzyme active center fluorescent probe)
RN 72006-37-2 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 3,5-dihydro-3-(5-O-phosphono-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

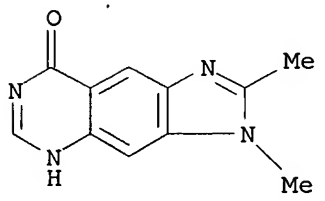
Absolute stereochemistry.



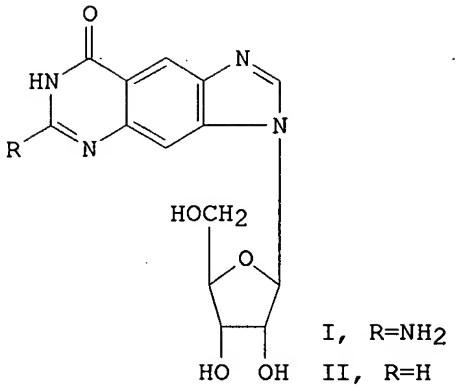
L4 ANSWER 76 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:523697 HCAPLUS
DOCUMENT NUMBER: 91:123697
TITLE: Synthesis of polynuclear heterocycles. Part 4. imidazo[4,5-g][3,1]benzoxazinones, imidazo[4,5-g]quinazolinones, imidazo[4,5-g]quinazolinediones, and imidazo[4,5-f]indazolinones
AUTHOR(S): Alkhader, Mohamed A.; Perera, R. Clinton; Sinha, Rajeshwar P.; Smalley, Robert K.
CORPORATE SOURCE: Dep. Chem. App. Chem., Univ. Salford, Salford, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1979), (4), 1056-62
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 91:123697

AB Several 1,2-disubstituted 6-aminobenzimidazole-5-carboxylic acids and their Et esters were prepared in several steps from 4,3-Cl(O2N)C6H3CO2Et. The amino acids reacted with acyl halides in pyridine to give 7-arylimidazo[4,5-g][3,1]benzoxazin-5-ones, with urea or KCN to give imidazo[4,5-g]quinazoline-5,7-diones, and with HCONH2 to give imidazo[4,5-g]quinazolin-5-ones. 6-Amino- and 6-(acylamino)imidazo[4,5-g]quinazolin-5-ones were prepared by treating the acylated amino esters with N2H4, or by cyclizing the derived aminohydrazides with an acylating agent. Imidazo[4,5-f]indazolin-5-ones were obtained by the action of ethanolic N2H4.H2O on 6-azido-5-ethoxycarbonylbenzimidazoles.

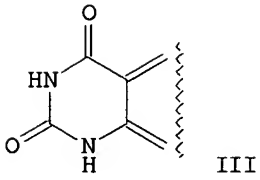
IT 71249-73-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 71249-73-5 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 3,5-dihydro-2,3-dimethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 77 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:508176 HCAPLUS
DOCUMENT NUMBER: 91:108176
TITLE: Synthesis of lin-benzoinosine, lin-benzoxanthosine, and lin-benzoguanosine
AUTHOR(S): Keyser, Gene E.; Leonard, Nelson J.
CORPORATE SOURCE: Roger Adams Lab., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Journal of Organic Chemistry (1979), 44(17), 2989-94
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=NH2
II, R=H



III

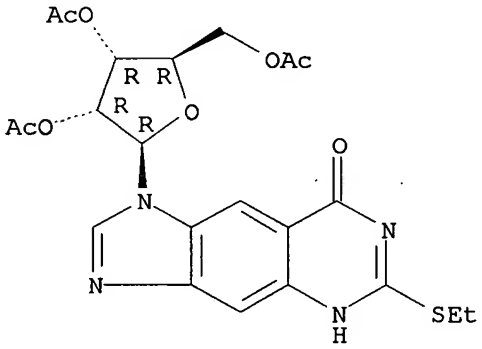
AB Ribosidation of the mercuric salt of 6-(ethylthio)imidazo[4,5-g]quinazolin-8-one gave a common intermediate in which the ethylthio group was displaced by NH3 to give lin-benzoguanosine (I) or was reductively removed to give lin-benzoinosine (II). II was oxidized by xanthine oxidase to give lin-benzoxanthosine (III).

IT 70631-19-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and desulfuration-deacetylation of)

RN 70631-19-5 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 6-(ethylthio)-1,5-dihydro-1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 78 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:204414 HCAPLUS

DOCUMENT NUMBER: 90:204414

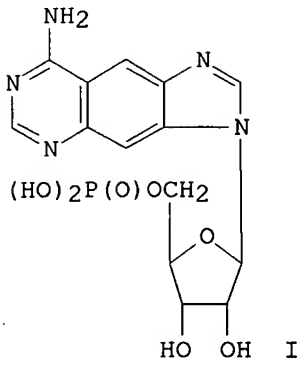
TITLE: lin-Benzoadenine nucleotides. Inter- and intramolecular interactions in aqueous solutions as observed by proton magnetic resonance

AUTHOR(S): Barrio, Jorge R.; Liu, Fu-Tong; Keyser, Gene E.; Van der Lijn, Pieter; Leonard, Nelson J.

CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA

SOURCE: Journal of the American Chemical Society (1979), 101(6), 1564-9
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal
LANGUAGE: English
GI

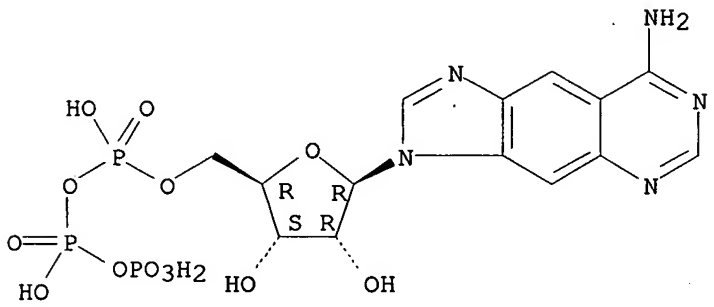


I

AB The inter- and intramol. interactions of lin-benzoadenine nucleotides, e.g., I, were examined by 1H-NMR. When the base is unprotonated, lin-benzoadenine nucleotides strongly stack in aqueous solution, with association consts. of at least one order of magnitude greater than those of the corresponding adenine nucleotides. Some head-to-tail orientations of stacked lin-benzoadenine nucleotides were indicated by the D substitution effect on relaxation times. The relative positions of the heteroarom. proton chemical shifts at infinite dilution (pD 8.5) and under acidic conditions (pD .apprx.4.0) indicted the conformations of the nucleotides (anti and syn, resp.) and the site of ring protonation (the pyrimidine ring).

IT 61925-58-4
RL: PRP (Properties)
(NMR of, inter- and intramol. interactions in aqueous solution in relation to)
RN 61925-58-4 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



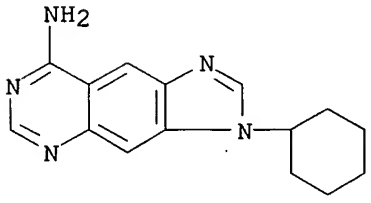
L4 ANSWER 79 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:35124 HCAPLUS
DOCUMENT NUMBER: 90:35124

10/ 715,547

TITLE: Spectroscopic sensitivity of linear-benzoadenine nucleotides to divalent metal counterions, side chain conformations, micelles, and enzymes
AUTHOR(S): VanDerLijn, Pieter; Barrio, Jorge R.; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1978), 75(9), 4204-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB From pKa data for lin-benzoadenosine 5'-mono, 5'-di, and 5'-triphosphates, which are fluorescent stretched-out analogs of adenine nucleotides, it was possible to designate the cases of interaction of phosphate with the heteroarom. moiety. The addition of divalent metal cations or quaternary ammonium micelles diminished the direct intramol. interaction between the phosphate(s) and base and consequently brought the pKa values close to that of lin-benzoadenosine. Fluorescence spectroscopy was used to investigate the interaction of lin-benzoadenine nucleotides with Mg2+, Mn2+, and Co2+. The association consts. for the formation of such complexes were obtained from measurements of steady-state fluorescence quenching. Phase and modulation measurements of the fluorescence lifetimes of lin-benzoadenine nucleotides as a function of Co2+ concentration permitted determination of the static component of the quenching due to intramol. complex formation. The association consts. of the lin-benzoadenine nucleotides with all of the divalent metal ions studied were greater than those observed for the corresponding adenine nucleotides and were in the order: lin-benzo-ATP > lin-benzo-ADP > lin-benzo-AMP. Fourier transform 1H NMR of lin-benzo-ATP in the presence of Co2+ showed broadening of the aromatic proton signals, the 2-H signal (corresponding to the 8-H in ATP) being the most affected. Models are proposed to explain the phosphate-base interaction, the influence of metal ions on base protonation, and the intramol. quenching observed in the complexes due to paramagnetic ion (Co2+ and Mn2+) and base interaction.

IT 53449-37-9
RL: PRP (Properties)
(fluorescence of, divalent cations and enzymes and quaternary ammonium micelles effect on)
RN 53449-37-9 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-cyclohexyl- (9CI) (CA INDEX NAME)



L4 ANSWER 80 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:18224 HCAPLUS
DOCUMENT NUMBER: 90:18224
TITLE: Allosteric activation of aspartate transcarbamylase with a fluorescent nucleotide analog: linear-benzo-ATP
AUTHOR(S): Van der Lijn, Pieter; Barrio, Jorge R.; Leonard, Nelson J.

CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA
SOURCE: Journal of Biological Chemistry (1978), 253(24), 8694-6
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

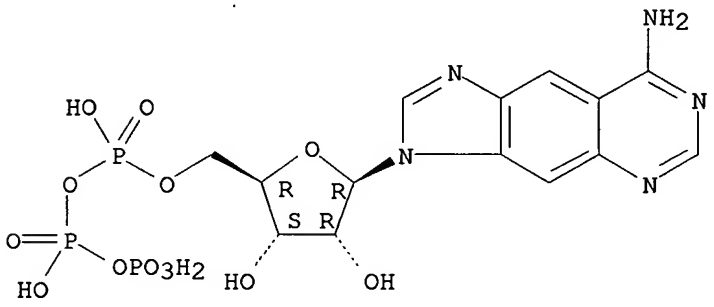
AB The interaction of Escherichia coli aspartate transcarbamylase (I) with linear-benzo-ATP (II) was investigated by fluorescence spectroscopy. The fluorescent nucleotide analog activated the enzyme to the same extent as ATP. Fluorescence polarization was used to determine the association constant of II with I which is 5 + 10-3 M-1 at pH 8.7, at 4°, assuming 6 binding sites. This association constant is similar to those previously obtained for ATP at a variety of temps., buffers, and pH. The fluorescence emission of II is not quenched when bound to I which indicates absence of π interactions between the activator and tyrosyl residues in the protein. These residues were implicated in the stereochem. mechanism of allosteric interactions in I. Furthermore, this fluorescence behavior indicates H-bond formation between the amino group of II and a nucleophilic center at the enzyme binding site. The fact that II activates I is consistent with a previously published model for nucleotide regulation of the enzyme.

IT 61925-58-4
RL: BIOL (Biological study)
(aspartate transcarbamylase allosteric activation by)

RN 61925-58-4 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 81 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:611011 HCAPLUS
DOCUMENT NUMBER: 89:211011
TITLE: Synthesis of modified nucleoside 3',5'-bisphosphates and their incorporation into oligoribonucleotides with T4 RNA ligase
AUTHOR(S): Barrio, Jorge R.; Barrio, Maria del Carmen G.; Leonard, Nelson J.; England, Thomas E.; Uhlenbeck, Olke C.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA
SOURCE: Biochemistry (1978), 17(11), 2077-81
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple procedure is described to prepare nucleoside 3'(2'),5'-diphosphates

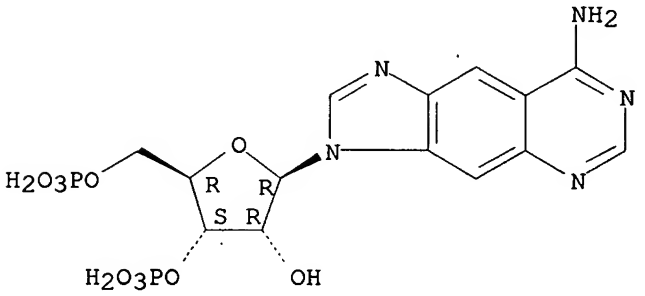
from the corresponding nucleosides with the use of pyrophosphoryl chloride. This method is rapid, gives nearly quant. yields and, most importantly, can be used for a variety of nucleosides with base and sugar modifications. Since 3',5'-diphosphates are donors in the phage T4 RNA ligase reaction, a single residue can be enzymically attached to the 3'-end of oligoribonucleotides. By these procedures, 5 different ring-modified nucleosides and 1 sugar-modified nucleoside were incorporated onto the 3'-end of (Ap)3C. In 2 cases, an addnl. step of synthesis with RNA ligase resulted in the modified nucleotide being located in an internal position in the oligonucleotide. Thus, a general method for the synthesis of oligoribonucleotides containing modified nucleosides is outlined. Since many of the modified nucleosides are fluorescent, oligomers containing them should be useful in a variety of phys. and biochem. studies.

IT 67126-60-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and phosphorus-31 NMR of)

RN 67126-60-7 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-(3,5-di-O-phosphono-β-D-ribofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 82 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:593114 HCAPLUS

DOCUMENT NUMBER: 89:193114

TITLE: Dimensional probes of the enzyme binding sites of adenine nucleotides. Interaction of lin-benzoadenosine 5'-di- and triphosphate with mitochondrial ATP synthetase, purified ATPase, and the adenine nucleotide carrier

AUTHOR(S): Kauffman, Raymond F.; Lardy, Henry A.; Barrio, Jorge R.; Barrio, Maria del Carmen G.; Leonard, Nelson J.

CORPORATE SOURCE: Inst. Enzyme Res., Univ. Wisconsin, Madison, WI, USA

SOURCE: Biochemistry (1978), 17(18), 3686-92
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The adenine nucleotide analogs, lin-benzo-ADP (I) and lin-benzo-ATP (II), were substrates for phosphorylation by submitochondrial particles and for hydrolysis by purified mitochondrial ATPase. A technique is described which simplified the kinetics of phosphorylation by submitochondrial particles. Substrate inhibition by inorg. phosphate (Pi) became apparent with I as the substrate for phosphorylation in the particles. Purified mitochondrial ATPase was inhibited more potently by I than by ADP. The fluorescence of I was strongly quenched by purified mitochondrial ATPase. With intact mitochondria, I was a poor acceptor for oxidative phosphorylation. Both the rate and extent of 32P1 incorporation into organic

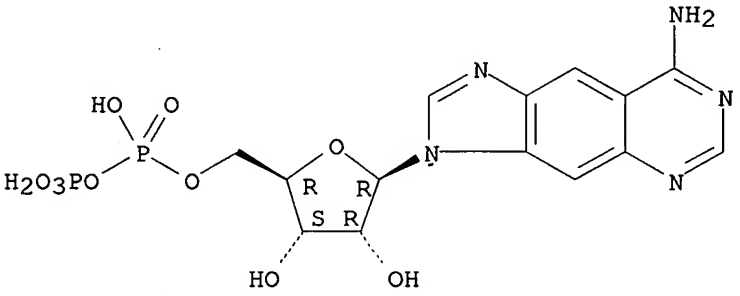
phosphates were enhanced only slightly by I, and this enhancement was completely sensitive to EDTA but not to fluoride. The ADP-stimulated respiration rate and the P/O ratio for these mitochondria were not affected by EDTA. I or II displaced only minute amts. of radioactivity from intact mitochondria loaded with ADP-14C. These data indicate that I and II displayed little, if any, activity as substrates for the adenine nucleotide carrier. The possibility that nucleoside diphosphokinase in the intermembrane space transferred phosphoryl-32P groups from endogenous ATP to I is discussed.

IT 61925-59-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with ATP synthetase, kinetics of)

RN 61925-59-5 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(phosphonooxy)phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 83 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:593113 HCAPLUS

DOCUMENT NUMBER: 89:193113

TITLE: Dimensional probes of the enzyme binding sites of adenine nucleotides. Biological effects of widening the adenine ring by 2.4 Å

AUTHOR(S): Leonard, Nelson J.; Scopes, David I. C.; Van der Lijn, Pieter; Barrio, Jorge R.

CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA

SOURCE: Biochemistry (1978), 17(18), 3677-85
CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal

LANGUAGE: English

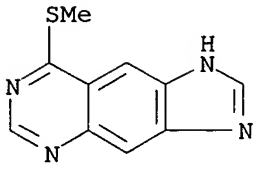
AB Lin-Benzoadenine nucleotides, defined by the formal insertion of a benzene ring (actually 4 C atoms) into the center of the purine system, were synthesized and their chemical integrity and purity analyzed by high performance liquid chromatog., paper electrophoresis, and 31P NMR. With these dimensional probes, the size restrictions of enzyme-active sites specific for purine cofactors were tested with respect to enzyme binding and activity. The stretched-out (by 2.4 Å) adenine nucleotide analogs bound strongly and had generally slower enzymic rates with a representative group of kinases, comprising pyruvate kinase, adenylate kinase, phosphofructokinase, phosphoglycerate kinase, hexokinase, and acetate kinase. Lin-Benzo-ADP acted as a substrate for primer independent polynucleotide phosphorylase (Micrococcus luteus) in the presence of Mn2+. The nucleotides also showed useful fluorescence properties and sensitivity to environmental conditions, e.g., divalent metal ions and stacking. The useful fluorescence properties of lin-benzoadenosine 5'-mono-, 5'-di-, 5'-tri-, and 3',5'-monophosphates and their increased π interactions can be directed to a variety of studies of static antidynamic interactions

with different moieties, complexations, the nature of enzyme binding sites, and conformational changes induced by surrogate coenzyme/enzyme binding.

IT 53449-20-0
RL: BIOL (Biological study)
(in lin-benzoadenosine preparation)

RN 53449-20-0 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline, 8-(methylthio)- (9CI) (CA INDEX NAME)



L4 ANSWER 84 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:525129 HCAPLUS

DOCUMENT NUMBER: 89:125129

TITLE: Effect of lin-benzoadenosine and lin-benzoadenosine 3':5'-monophosphate on cyclic AMP-dependent protein kinase activity in vitro

AUTHOR(S): Schmidt, M. J.; Truex, L. L.; Leonard, N. J.; Scopes, D. I.; Barrio, J. R.

CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, USA

SOURCE: Journal of Cyclic Nucleotide Research (1978), 4(3), 201-7
CODEN: JCNRDU; ISSN: 0095-1544

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The fluorescent stretched-out analog of cyclic AMP, linear-benzoadenosine 3',5'-monophosphate, maximally activated brain protein kinase and protein kinase from skeletal muscle. The corresponding linear-benzoadenosine inhibited kinase activity slightly less than did adenosine. Thus, the 2.4 Å-wider derivs. of cyclic AMP and of adenosine interact with protein kinase in a manner similar to that of the natural compds.

IT 67715-94-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

RN 67715-94-0 HCAPLUS

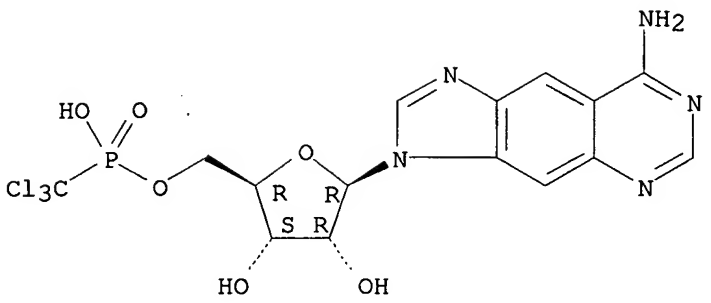
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy(trichloromethyl)phosphinyl]-β-D-ribofuranosyl]-, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 67715-93-9

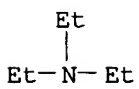
CMF C15 H15 Cl3 N5 O6 P

Absolute stereochemistry.



CM 2

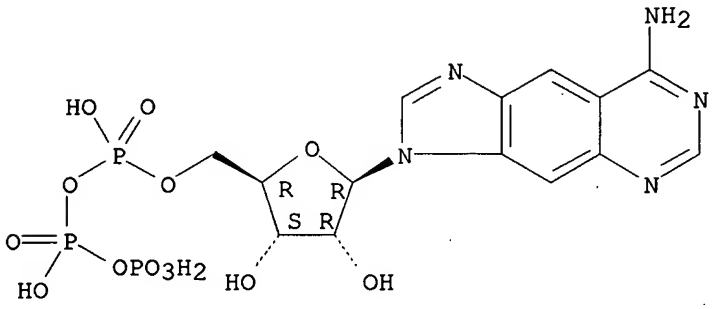
CRN 121-44-8
CMF C6 H15 N



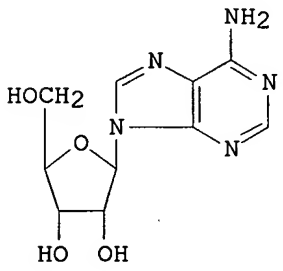
L4 ANSWER 85 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:438583 HCAPLUS
DOCUMENT NUMBER: 89:38583
TITLE: An enzyme system for the replication of duplex circular DNA. The replicative form of phage .vphi.X174. 6. ATP utilization by rep protein in the catalytic separation of DNA strands at a replicating fork
AUTHOR(S): Kornberg, Arthur; Scott, John F.; Bertsch, LeRoy L.
CORPORATE SOURCE: Dep. Biochem., Stanford Univ. Sch. Med., Stanford, CA, USA
SOURCE: Journal of Biological Chemistry (1978), 253(9), 3298-304
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hydrolysis of ATP by rep protein proceeds in the presence of a single-stranded region of DNA 4 residues long, but the true effector for rep ATPase appears to be a replicating fork rather than a random coil. At or near a fork in duplex DNA, rep ATPase action is different from what it is on DNA lacking secondary structure (single-stranded): (1) Km for ATP is lower, (2) specificity is for ATP and dATP with no action on other nucleoside triphosphates, (3) sensitivity to certain ATP analogs is reduced, (4) presence of a DNA-nicking enzyme (e.g. cistron A protein induced by .vphi.X174) is required, and (5) Escherichia coli DNA-binding protein facilitates rather than inhibits. During the separation of strands accompanying replication, 2 mols. of nucleoside triphosphate (ATP or dATP) are hydrolyzed for every nucleotide polymerized Utilization of ATP by rep protein may provide energy for catalytic strand separation at a fork in advance of replication.
IT 61925-58-4
RL: BIOL (Biological study)
(as DNA-dependent ATPase substrate)
RN 61925-58-4 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy

)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 86 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:400965 HCAPLUS
DOCUMENT NUMBER: 89:965
TITLE: Ligand binding to the adenine analog binding protein of the rabbit erythrocyte
AUTHOR(S): Olsson, R. A.
CORPORATE SOURCE: Coll. Med., Univ. South Florida, Tampa, FL, USA
SOURCE: Biochemistry (1978), 17(2), 367-75
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



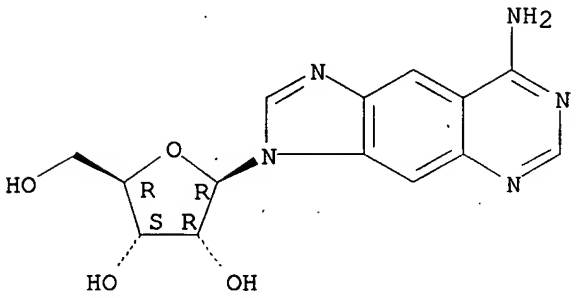
I

AB Adenine analog binding protein of rabbit erythrocytes reversibly bond tritium-labeled adenosine (I) [68-94-0] with an equilibrium constant of 5.3 + 10-9M, an association rate constant of 1.4 + 10-12M-1 min-1, and a dissociation rate constant of 7.5 + 10-3 min-1, as estimated by anonlinear curve-fitting program applied to data on the time course of the binding reaction. Inhibition of I binding by a series of 77 I analogs was used to define the factors determining the binding affinity of this nucleoside. These are:(1) the size and aromaticity of the purine base:(2) a glycosylic torsion angle of .apprx.-120°; (3) the ribo configurationof the 2'- and 3'-hydroxyls and also the 5'-hydroxyl. Bulky substituents in the region of C-2' and to a lesser extent in the region of C-3' decreased affinity.
IT 60189-62-0
RL: PRP (Properties)
(adenosine binding by protein inhibition by, in erythrocyte)
RN 60189-62-0 HCAPLUS

10/ 715,547

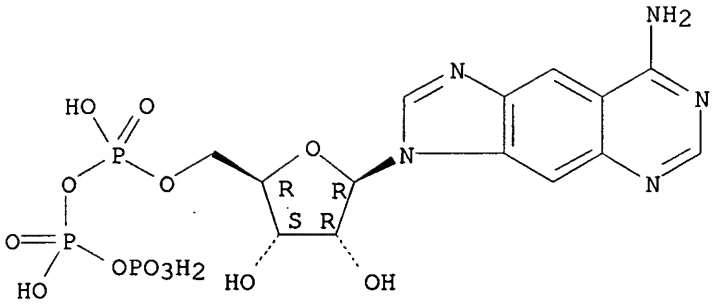
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-β-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

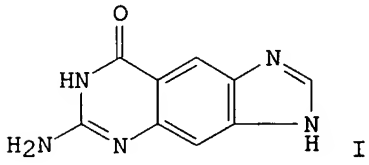


L4 ANSWER 87 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:67391 HCAPLUS
DOCUMENT NUMBER: 86:67391
TITLE: Defined dimensional changes in enzyme cofactors: fluorescent "stretched-out" analogs of adenine nucleotides
AUTHOR(S): Scopes, David I. C.; Barrio, Jorge R.; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA
SOURCE: Science (Washington, DC, United States) (1977), 195(4275), 296-8
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A concept is presented for testing the dimensional restrictions of enzyme-active sites by stretching the substrate or cofactor by known magnitude. These restrictions of enzyme-active sites specific for purine cofactors were tested by the synthesis and evaluation of lin-benzoadenosine 5'-triphosphate, 5'-diphosphate, and 3',5'-monophosphate with respect to enzyme binding and activity. These stretched-out (by 2.4 Å) versions of the adenine ribonucleotides bind strongly, slow the enzymic rates, and have useful fluorescence properties.
IT 61925-58-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(coenzyme activity of)
RN 61925-58-4 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine, 3-[5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-β-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



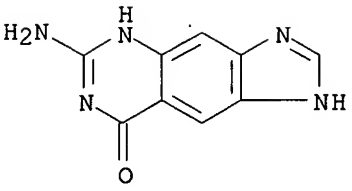
L4 ANSWER 88 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:577355 HCAPLUS
DOCUMENT NUMBER: 85:177355
TITLE: Linear benzoguanine. Synthesis by two independent methods
AUTHOR(S): Keyser, Gene E.; Leonard, Nelson J.
CORPORATE SOURCE: Roger Adams Lab., Univ. Illinois, Urbana, IL, USA
SOURCE: Journal of Organic Chemistry (1976), 41(22), 3529-32
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

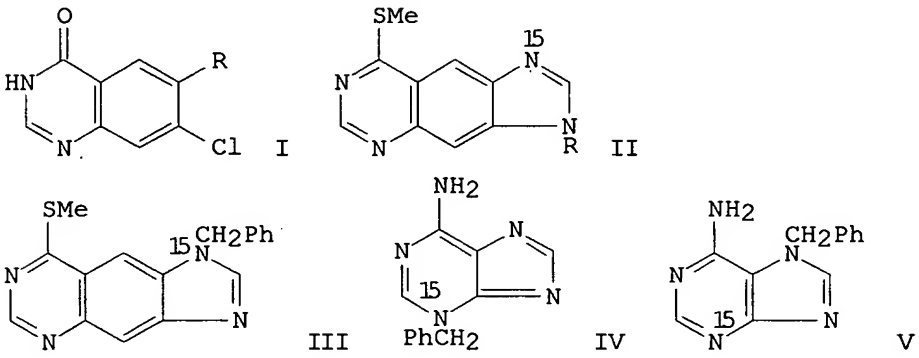
AB Benzoguanine, 6-aminoimidazo[4,5-a]quinazol-8-one (I), was synthesized by two independent methods, both starting with an intact central benzenoid ring. In 1 route, the substituted benzimidazole moiety was elaborated before closure of the pyrimidine ring. In the other, the substituted quinazolone was synthesized prior to imidazolee ring closure. I is fluorescent and represents a version of guanine that is widened by 2.4 Å.

IT 60064-30-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 60064-30-4 HCAPLUS
CN 8H-Imidazo[4,5-g]quinazolin-8-one, 6-amino-1,7-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L4 ANSWER 89 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:523850 HCAPLUS
DOCUMENT NUMBER: 85:123850
TITLE: Nitrogen-15-carbon-13 coupling for determination of the site of N-alkylation of nitrogen heterocycles. linear-Benzopurines
AUTHOR(S): Wiemer, David F.; Scopes, David I. C.; Leonard, Nelson J.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA
SOURCE: Journal of Organic Chemistry (1976), 41(18), 3051-3
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

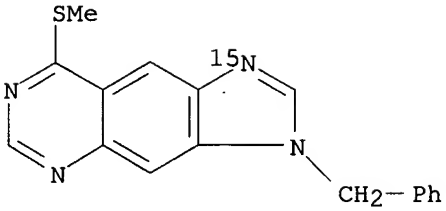


AB 7-Chloro-4-quinazolone I (R = H) was nitrated with H15NO3 and the I (R = 15NO2), converted to the imidazoquinazoline II (R = H), which was benzylated with PhCH2Br to give II (R = PhCH2) and III. The structures were confirmed by 15N-13C coupling of the benzylic C. IV and V were prepared as model compds.

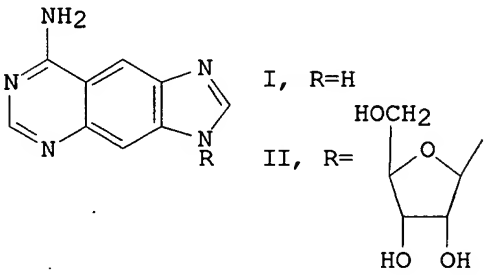
IT 59710-63-3P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and NMR of)

RN 59710-63-3 HCAPLUS

CN 3H-Imidazo[4,5-g]quinazoline-1-15N, 8-(methylthio)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 90 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1976:489129 HCAPLUS
DOCUMENT NUMBER: 85:89129
TITLE: Defined dimensional changes in enzyme substrates and cofactors. Synthesis of lin-benzoadenosine and enzymic evaluation of derivatives of the benzopurines
AUTHOR(S): Leonard, Nelson J.; Sprecker, Mark A.; Morrice, Alan G.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA
SOURCE: Journal of the American Chemical Society (1976), 98(13), 3987-94
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



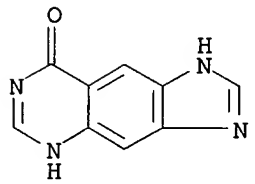
AB A biochem. evaluation of derivs. of 8-aminoimidazo[4,5-g]quinazoline (I), 9-aminoimidazo[4,5-f]quinazoline, and 6-aminoimidazo[4,5-h]quinazoline, stretched-out versions of adenine which are given the descriptive names lin-, prox-, and dist-benzoadenine, resp., is reported, along with the synthesis of lin-benzoadenosine (II), the ribonucleoside of I. The synthesis of II involves the reaction of tri-O-acetyl-D-ribofuranosyl bromide with 8-methylthioimidazo[4,5-g]quinazoline in the presence of mercuric cyanide to afford 2 methyllthioribofuranosides which, when treated with ethanolic NH3, are converted to II and an isomeric compound, 1-β-D-ribofuranosyl-lin-benzoadenine. II and the active cytokinin analogs, N8-benzyl-lin-benzoadenine and N8-(Δ2-isopentenyl)-lin-benzoadenine, exhibit potentially useful fluorescence properties. II is hydrolyzed to lin-benzoinosine (III) by adenosine deaminase at a relative rate comparable to that for the conversion of adenosine to inosine. Surprisingly, adenosine deaminase also promotes conversion of I to lin-benzohypoxanthine (IV); the isomeric nonlinear benzoadenines are refractory. Xanthine oxidase converts IV to lin-benzoxanthine and lin-benzouric acid. III is oxidized to the corresponding ribonucleosides, namely lin-benzoxanthosine and 3-(β-D-ribofuranosyl)-lin-benzouric acid. Prox-benzohypoxanthine reacts with xanthine oxidase at a slow

relative rate to afford prox-benzoxanthine and prox-benzouric acid. Dist-benzohypoxanthine is oxidized to the 1st stage, dist-benzoxanthine. Nucleoside phosphorylase does not promote glycosidic cleavage of II or III, and adenine phosphoribosyltransferase does not accept the benzoadenines as substrates. The activity, or lack of activity, of the benzopurine derivs. with the selected enzymes demonstrates the successful application of the concept of testing the dimensional restrictions of enzyme active sites by lateral stretching (by 2.4 Å in the case of the lin-benzopurines) of the normal substrates.

IT 53449-18-6
RL: BIOL (Biological study)
(adenine deaminase and xanthine oxidase specificity for)

RN 53449-18-6 HCAPLUS

CN 8H-Imidazo[4,5-g]quinazolin-8-one, 1,5-dihydro- (9CI) (CA INDEX NAME)



L4 ANSWER 91 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1976:446584 HCAPLUS

DOCUMENT NUMBER: 85:46584

TITLE: Fluorescent cytokinins: stretched-out analogs of N6-benzyladenine and N6-(Δ2-isopentenyl) adenine

AUTHOR(S): Sprecker, Mark A.; Morrice, Alan G.; Gruber, Bruce A.; Leonard, Nelson J.; Schmitz, Ruth Y.; Skoog, Folke

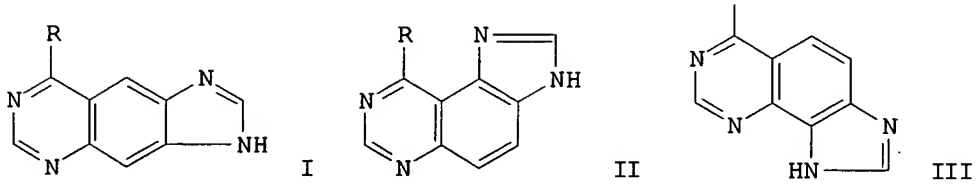
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA

SOURCE: Phytochemistry (Elsevier) (1976), 15(5), 609-13
CODEN: PYTCAS; ISSN: 0031-9422

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

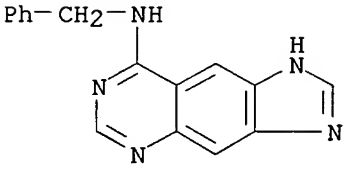


I II III

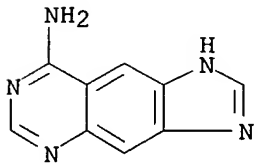
AB The fluorescent imidazoquinazolines I-III (R = NHCH2CH:CMe2, NHCH2Ph) were prepared by treating I-III (R = SH) with H2NR and their cytokinin activities were determined by the tobacco bioassay. I (R = NHCH2CH:CMe2, NHCH2Ph) are active, II and III (R = NHCH2CH:CMe2) are slightly active, and II and III (R = NHCH2Ph) are inactive.

IT 53449-32-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cytokinin activity of)

RN 53449-32-4 HCAPLUS
CN 1H-Imidazo[4,5-g]quinazolin-8-amine, N-(phenylmethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 92 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:547454 HCAPLUS
DOCUMENT NUMBER: 83:147454
TITLE: Benzoadenines. Synthesis of stretched-out analogs of adenine
AUTHOR(S): Morrice, Alan G.
CORPORATE SOURCE: Univ. Illinois, Urbana, IL, USA
SOURCE: (1974) 84 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 75-11,588
From: Diss. Abstr. Int. B 1975, 35(11), 5340-1
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT 53449-12-0DP, 1H-Imidazo[4,5-g]quinazolin-8-amine, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 53449-12-0 HCAPLUS
CN 3H-Imidazo[4,5-g]quinazolin-8-amine (CA INDEX NAME)



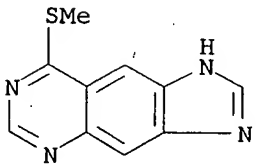
L4 ANSWER 93 OF 93 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:97991 HCAPLUS
DOCUMENT NUMBER: 82:97991
TITLE: Linear benzoadenine. Stretched-out analog of adenine
AUTHOR(S): Leonard, Nelson J.; Morrice, Alan G.; Sprecker, Mark A.
CORPORATE SOURCE: Sch. Chem. Sci., Univ. Illinois, Urbana, IL, USA
SOURCE: Journal of Organic Chemistry (1975), 40(3), 356-63
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The synthesis of 8-aminoimidazo-[4,5-g]quinazoline (I), an extended version of adenine which is called lin-benzoadenine, is reported. 7-Chloro-4-quinazolone II was converted into imidazo[4,5-g]quinazolin-8-one (III) in 4 steps, followed by thiation to 8-mercaptoimidazo[4,5-g]quinazoline and subsequent replacement of the thiol function by ammonia to yield the linear benzoadenine isomer I. The aralkyl derivs. of I,

e.g., 8-amino-1- and 3-benzylimidazo[4,5-g]quinazoline, which serve as uv models in assigning the structure of nucleoside and nucleotide targets and to direct further substitution, were obtained indirectly via benzylation of 8-(methylthio)-imidazo[4,5-g]quinazoline. A general comparison of the uv spectra of various 8-(methylthio)- and 8-aminoimidazo[4,5-g]-quinazoline derivs. in neutral, acidic, and basic solution indicates that first protonation occurs mainly on the imidazole ring of the methylthio compds. and on the quinazoline ring of the amino compds.

IT 53449-20-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation of)

RN 53449-20-0 HCAPLUS

CN 1H-Imidazo[4,5-g]quinazoline, 8-(methylthio)- (9CI) (CA INDEX NAME)



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